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VOLUME 39 (OLD SERIES VOLUME 98) NUMBER 4

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APRIL 1948

PUBLISHED MONTHLY BY AMERICAN MEDICAL ASSOCIATION, 535 NORTH DEARBORN STREET, CHICAGO 10, ILLINOIS. ANNUAL SUBSCRIPTION, $10.00

Entered as Second Class Matter Feb. 7, 1929, at the Postoffice at Chicago, Under the Act of Congress of March 3, 1879. Additional entry at Nashville, Tenn.

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Archives of Ophthalmology

VOLUME 39 (old series Volume 96) APRIL 1948 NUMBER 4

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AMERICAN OPHTHALMOLOGY DURING THE PAST CENTURY

F. H. VERHOEFF, M.D.
BOSTON

Acceptance of the invitation to be your guest at this memorable meeting of the American Medical Association imposed on me the duty of addressing you on the subject of the history of american ophthalmology. In view of this terrifying obligation, my presence here attests my profound appreciation of the honor you have conferred on me. The address to which I have given birth after much labor, I fear is but a mouse. Although largely about ophthalmologists of the past, it is not an obituary, for in it I try to speak the truth, the whole truth and nothing but the truth. To relieve any anxiety this statement may arouse, I hasten to add that no ophthalmologist now in active practice is mentioned by name.

One hundred years ago there were, strictly speaking, no ophthalmologists. However, there were a few doctors here and there who devoted an unusually large part of their practice to diseases of the eye and hence may be called part time ophthalmologists. It is not clear whether they became such by their own choice or by choice of the public. As to the mother of american ophthalmology, histories are silent; but Elisha North (1771-1843), of New London, Conn.; Philip Syng Physick (1768-1837), of Philadelphia, and George Frick (1793-1870), of Baltimore, each has been designated the father. In 1847 only one of these alleged parents was alive, and he had retired from practice. Of the part time ophthalmologists who were then in active practice the most notable were, in Philadelphia, William Gibson (1788-1868), Isaac Hays (1796-1879), William E. Horner (1793-1853) and Squier Littell (1803-1880); in Louisville, Ky., Samuel D. Gross (1805-1884); in Baltimore, Nathan R. Smith (1797-1877); in Boston, Edward Reynolds (1793-1881), John Jeffries (1796-1876) and John H. Dix (1813-1884); in New York, Edward Delafield (1795-1875), William Clay Wallace and Alfred C. Post (1806-1886).

To American doctors of 1847, two American textbooks on diseases of the eye were available, one (1823) by George Frick[1] and the other

Read before the Section on Ophthalmology, at the Ninety-Sixth Annual Session of the American Medical Association, Atlantic City, June 12, 1947.

(1837) by Squier Littrell.[2] These were largely based on Beer's German textbook[3] of 1817. Also available were several British textbooks, the best of which was the "Practical Treatise on Disease of the Eye" (1830)[4] by William Mackenzie of Glasgow, Scotland. The gross structure of the eye was relatively well known, and something was even known as to the histology of the eye. James Wardrop, of Scotland, later of London, in 1808 had classified and named diseases of the eye according to the structures chiefly involved. Thus, he was the first to use the term keratitis. What was known in 1847 concerning diseases of the eye is revealed by perusal of the textbooks mentioned. The chief topics in Littell's textbook were diseases of the orbit, including tumors, and aneurysm by anastomosis (for which ligation of the carotid artery was advised); diseases of the lacriymal organs, inflammation of the eyelids, syphilitic infections of the eyelids, tumors of the eyelids, hordeoleum, ankyloblepharon, symblepharon, ectropion, entropion, trichiasis, distichiasis, lagophthalmos, ptosis, conjunctivitis, "varolus ophthalmicus," pterygium, xerosis, acute corneitis, pannus, abscess of the cornea, ulcer of the cornea, staphyloma of the cornea, conical cornea, sclerotitis, choroiditis, retinitis, iritis, cataract, hydrophthalmos, glaucoma, cancer of the eye, melanosis (malignant melanoma), fungus hematoides (retinoblastoma), paralaysis of muscles of the eye, day blindness, night blindness, amaurosis, muscae volitantes, strabismus, myopia and presbyopia. It is interesting, that although thirty-two years were to elapse before the discovery of the gonococcus, it was known that purulent conjunctivitis was sometimes caused by gonorrheal infection. A form of keratitis due to heridatary syphilis had not been recognized, for Hutchinson had not yet made his great contributions to ophthalmology. The term amaurosis was used to hide ignorance of many conditions with which one is now familiar. Retinitis and choroiditis were known to occur, but in actual cases their existence could only be guessed at, for the ophthalmoscope had not yet been developed.[5]

Perimetry had not come into being, and refraction tests were not made—no doctor possessed a trial case of lenses. Glasses were not pre-

1. Frick, G.: A Treatise on the Diseases of the Eye; Including the Doctrines and Practice of the Most Eminent Modern Surgeons, and Particularly Those of Professor Beer, Baltimore, F. Lucas, Jr., 1823.

2. Littell, S., Jr.: A Manual of the Diseases of the Eye, Philadelphia, J. S. Littell, 1837.

3. Beer, G. J.: Lehre von den Augenkrankheiten, als Leitfaden zu seinon offentlichen Vorlesungen entworfen, Vienna, Camesina, Huebner u. Volke, 1813-1817.

4. Mackenzie, W.: A Practical Treatise on the Diseases of the Eye, London, Longman, [and others], 1830.

5. It is interesting to note that 1847 was the year that Bakkage demonstrated his model of the ophthalmoscope to the English ophthalmologist Wharton Jones, who rejected it. It was not until four years later that von Helmholtz, independently, invented another model and established its significance.

scribed by physicians but were fitted at the discretion of opticians. Cylindric lenses were not yet available. Ether anesthesia was just coming into general use, but local anesthesia was unknown. Operations were done on the lids for entropion, ectropion, and the like, but the only important operations on the eyeball itself were discission of cataract, extraction of cataract, making of an artificial pupil and enucleation. Paracentesis for glaucoma was sometimes done, but the value of iridectomy for this condition was still unknown.

Atropine was used to combat iritis, but the antiglaucomatous effects of physostigmene and pilocarpine had not yet been discovered. Some of the drugs employed in collyriums, ointments or powders may be noted: mercury in several forms, including mercury bichloride; silver nitrate; zinc sulfate; zinc oxide; copper sulfate; lead subacetate; tincture of iodine; sodium borate; camphor, and opium. Strychnine, quinine, oil of turpentine, preparations of iron, and tincture of colchicum seed were among the drugs given by mouth. Cathartics were regarded as highly important in the treatment of many conditions. Venesection was freely employed for almost all serious ocular conditions, including iritis. Setons, blistering agents and leeches were also frequently employed. I can recall that as late as 1900 leeches were kept on hand at the Massachusetts Eye and Ear Infirmary and were frequently used by the older surgeons. They were usually applied to the temple and were believed to allay pain and assist in dilatation of the pupil in cases of iritis. Their use has died out without being openly condemned by any one. Since leeches add something to the blood which hinders its coagulation, possibly they did have beneficial effect on certain inflammatory conditions. Littell stated that it was often impossible to distinguish syphilitic from diopathic iritis, but that this was unimportant, since the same treatment was used for the two diseases.

From what I have said, it is obvious that in 1847 ophthalmology was in a highly primitive state. This was especially so in America, for here medical education in general was woefully inadequate. In those days, and for many years afterward, specialism was frowned on by the medical profession. Even in 1864, when the American Ophthalmological Society was founded, many of its members, including its first president, Edward Delafield, practiced general medicine or surgery along with opththalmology. Moreover, from 1868 until within recent years this society had a rigid rule excluding from membership any one who in any public way designated himself a specialist. Its purpose was to prevent the public from assuming that oculists were not physicians. Only a few years ago, for the same reason, the term "eye physician" was suggested as a substitute for ophthalmologist or oculist.

However, in spite of the lack of real specialists in 1847, three special hospitals had already been founded and were in active operation, namely, the New York Eye Infirmary (1820), the Massachusetts Charitable Eye

and Ear Infirmary (1824) and the Wills Eye Hospital (1834). These hospitals were founded because of the meager facilities provided for the specialties in general hospitals. Such complete isolation of the specialties has proved to be unwise; for this reason the Massachusetts eye and Ear Infirmary, originally a completely independent institution, has become closely affiliated with the adjacent Massachusetts General Hospital.

The first American to restrict his practice exclusively to ophthalmology was Henry W. Williams (1821-1895). He did this in Boston a few years after his graduation from Harvard Medical School. He entered this school in 1844, but after two years went to Europe, where for three years he studied ophthalmology in addition to general medicine. He then returned to Harvard and obtained his medical degree in 1849. Throughout the greater part of his active life he remained the foremost American ophthalmologist of his day, and in 1871 he became the first professor of ophthalmology at the Harvard Medical School. On his retirement, in 1891, he endowed the professorship, which was then given his name. This, however, was not the first chair of opthalmology to be established in this country, for in 1860 Miami Medical College had created such a chair for an almost equally eminent specialist, Elkanah Williams (1822-1888), of Cincinnati, who is also given credit for being the first to restrict his practice to diseases of the eye, ear, nose and throat. These men were not brothers, as sometimes has been assumed, or, so far as is known, even distantly related. In 1862 Henry Williams published an ophthalmologic textbook[6], which passed through several editions, the last in 1866, and which was far superior to the three American textbooks that had preceded it. He was well thought of by his colleagues outside of Boston, as evidenced by the fact that he was one of the original members of the American Ophthalmological Society and its president from 1869 to 1873. He was president of the Massachusetts Medical Society in 1880 and was a fellow of the American Academy of Arts and Sciences, unusual honors for an ophthalmologist. He was a member of several exclusive social clubs in Boston and a member of the Eastern Yacht Club. Nevertheless, he was heartily disliked by his ophthalmologic colleagues in Boston. I have no printed evidence to this effect, but my information comes by word of mouth from a source in which I have complete confidence. From the same source I learn that the cause of this animosity was not jealousy on the part of his colleagues, but an autocratic attitude on the part of Williams. The facts that he was not a member of the New England Ophthalmological Society, organized in 1884, and that he was never on the staff of the Massachusetts Eye and Ear Infirmary accord with this information. That he could make remarkable headway in spite of such local hostility is additional evidence of his great professional ability.

6. Williams, H. W.: A Practical Guide to the Study of the Diseases of the Eye: Their Medical and Surgical Treatment, Boston, Ticknor & Fields, 1862.

Other prominent American ophthalmologists of the past century were Edward L. Holmes (1828-1900), Cornelius Rea Agnew (1830-1888), Herman Jakob Knapp (1832-1911), Henry Drury Noyes 1832-1900), Simon Pollak (1832-1913), George T. Stevens (1832-1921), John Green (1935-1913), Hasket Derby (1835-1914), George C. Harlan 1835-1909), Edward G. Loring (1837-1888), David Bennet St. John Roosa (1838-1908), William Fisher Norris (1839-1901), Emil Grüning (1842-1914), Leartus Conner (1843-1911), F. K. Hotz (1843-1908), Samuel Theobald (1846-1930), John E. Weeks (1853-), Charles H. Beard (1855-1916), Edward Jackson (1856-1942), Casey A. Wood (1856-1942), Alexander Duane (1858-1926), George E. de Schweinitz (1858-1938), and William C. Posey (1866-1934). There were many less well known ophthalmologists whose accomplishments, I am sure, were as great as, or greater than those of some of the men just listed.

The examples set by most of these prominent ophthalmologists as to devotion to their specialty, hard work and ethical conduct served to raise the standards of ophthalmology in this country. Probably highest in the esteem of their colleagues were Knapp, de Schweinitz and Jackson. Knapp was born in Germany and received his ophthalmologic training there. Leaving, at the age of 38, a professorship in Heidelberg, he moved to New York in 1868, where he spent the rest of his long and productive life. He gained prompt recognition as the preeminent ophthalmologist in America and did much to improve the status of his specialty here. He also specialized in otology, but not in laryngology. He founded a hospital, the New York Ophthalmic and Aural Institute, and also a journal, the *Archives of Ophthalmology and Otology* (1869), which, except for the short-lived and ill famed first *American Journal of Ophthalmology*, published by Julius Homberger, was the first ophthalmologic journal in America. The *Archives* has never been exceeded in importance by any other American ophthalmologic journal and has greatly contributed to the progress of ophthalmology in this country. In 1879 the *Archives of Otology* was separated from it.

De Schweinitz was lavishly endowed both physically and mentally. He had an imposing, yet charming, personality and was the handsomest ophthalmologist I have ever known. He was the most fluent speaker I have ever heard, and at the same time one of the clearest. He had a thorough knowledge of ophthalmic literature and often called on this at a moment's notice in discussing papers at medical meetings. He gained such wide recognition that he was elected president of the American Medical Association in 1916. In spite of his many distinctions, he was unassuming in his attitude and was generous in his praise of his colleagues. If he was lacking in any desirable qualities, they were dexterity and originality.

Jackson had the welfare of ophthalmology deeply at heart and did much to further it. The American Board of Ophthalmology was his

brainchild, as I shall explain later. As editor of the *American Journal of Ophthalmology,* he performed for many years valuable service. His broad knowledge of the sciences basic to ophthalmology was impressive and was often manifested in his editorials. Thus, although he had no first hand knowledge of pathologic anatomy, he had in some way acquired a remarkably accurate understanding of this subject.

Most of the eminent American ophthalmologists who have been in active practice within the past fifty years I have had the pleasure of knowing personally. But, of the older men, the one I knew best and to whom I am indebted for my initiation into ophthalmology was Samuel Theobald. He was the first professor of ophthalmology at Johns Hopkins Medical School, and I was his first pupil to become an ophthalmologist. He was the leading ophthalmologist and otologist in Baltimore and was elected president of the American Ophthalmological Society in 1910. I never heard him display any pride in his own accomplishments, but he often proudly referred to his grandfather, Nathan R. Smith. Theobald made two valuable contributions to ophthalmology. One was his demonstration that stricture of the lacrimal duct could be permanently overcome by the repeated insertion of very large probes. At each visit the probe was left in place for about thirty minutes, so that in his waiting room there was almost always the alarming spectacle of at least one patient with a probe protruding from the region of his eye. He taught some patients to probe their own ducts. I can vouch for the fact that this treatment was eminently successful, curing not only the chronic dacryocystitis but also the epiphora. The method, however, has never come into general use, doubtless for the reason that few ophthalmologists have been bold enough to use such large probes, or persuasive enough to induce patients to continue the treatment. Theobald's other valuable contribution was his discovery of what, for the lack of a better term, he called subnormal accommodation in young persons. He meant by this that the range of accommodation was diminished but that in certain persons so much effort was required to accommodate that it caused a considerable degree of esophoria at the reading distance. He found that the resulting discomfort was completely relieved by the use of presbyopic glasses. Today this condition seems to be generally neglected.

Three national ophthalmologic societies, the American Ophthalmological, the Section on Ophthalmology of the American Medical Association, and the American Academy of Ophthalmology and Otoloryngology, have reflected the progress of ophthalmology in this country and, in fact, have also greatly contributed to it. The American Ophthalmological Society was conceived by and organized in 1869 by the efforts of Henry D. Noyes, of New York, and Hasket Derby, of Boston. This was the first special medical society in America, and the second in the world. Although many important papers have been presented at its meetings, I think its major contribution to ophthalmology has been its high requirements for mem-

bership. Ever since its inception these requirements have included excellent professional performance and adherence to the highest professional ethics. Membership in the society has therefore been a laudable ambition for the young and a gratifying reward for the older ophthalmologist. Since it is human to err, the society has made mistakes of omissions and commissions in regard to membership, but these have been remarkably few.

Although at the meeting in 1863 the American Medical Association recognized ophthalmology as a distinct specialty, it included this in the Section on Surgery and Anatomy until 1878, when a section for ophthalmology, otology and laryngology was organized and called Section 6. Herman Knapp, on motion of Eugene Smith, of Michigan, was elected chairman. This election shows the rapidity with which Knapp had gained the high regard of his colleagues in his adopted country. At the Section's first meeting, covering three days, there were six papers relating to ophthalmology, three of which were on cataract operations; two papers relating to otology and one relating to laryngology. No transcripts of the discussions were kept, but in the minutes Knapp was mentioned as taking part in the discussions. In addition, he read his chairman's lengthy address on the progress of ophthalmology and otolgy, a paper on cataract operations and another on mastoid operations and demonstrated several microscopic specimens of the eye and one of a tumor of the acoustic nerve. It would seem that Knapp took a prominent part in the meeting, to say the least.

In 1888 the American Medical Association divorced ophthalmology from the other specialties and gave it a section all its own. I think it is fair to say that this section has been more progressive and original than any other section in the Association. Thus, in 1891, Leartus Conner, in his chairman's address, was the first to propose that each section publish its own transactions in a separate volume. This proposal was at once adopted by his own section. Previously, the transactions of all the sections had been included in the published transactions of the American Medical Association until the advent of *The Journal of the American Medical Association*, in 1883, when they were published in this. Incidentally, it may be mentioned that Samuel D. Gross, a part time ophthalmologist, suggested as far back as 1869 that the American Medical Association publish a journal. Conner also proposed two other innovations that were adopted; the election of the chairman by the section itself and the formation of an executive committee, such as we now have.

In 1905 this section originated a procedure of publishing the papers in advance of the meeting. This procedure had much merit, since it ensured better discussions, but was discontinued in 1932 on account of the expense involved and the difficulty of getting the volume printed before the meeting. However, in dying, the presessional volume left two important offspring, namely, the printing of full abstracts in the program, and

the selection of two speakers in advance to open the discussion of each paper.

Another innovation by this section was the establishment, in 1910, of the Knapp testimonial fund and the Knapp Medal, at the original suggestion of W. C. Posey. The medal was to be awarded to the author of the best paper presented at a meeting, provided the paper was of sufficiently high merit. The first award was made in 1914 to Clifford B. Walker. That a rather high standard has been set for the award is indicated by the fact that it has been made only eight times. Still another innovation was the establishment of the Ophthalmic Research Medal, at the suggestion of Lucien Howe, who in 1924 donated a fund of $1,500 to provide for it. This medal has been awarded ten times; the first recipient was Edward Jackson, in 1926; the second, George de Schweinitz, in 1927. It is noteworthy, and I think praiseworthy, that the Section did not designate this medal by the name of the donor. To have done so might have suggested that the Knapp medal was donated by Knapp.

An important enterprise sponsored by this Section and the other two national ophthalmologic Societies is the Registry of Ophthalmic Pathology at the Army Medical Museum. This was established in 1922, chiefly through the efforts of Harry Gradle and the cooperation of Major G. R. Callender. It has partly overcome the distressful, not to say disgraceful, waste of pathologic eye material in this country, and is now a rich storehouse of sections of the eye. This was the first registry at the Army Medical Museum, and not until several years later was the first of the numerous other registries organized.

Perhaps the greatest single achievement of this Section was the part it played in establishing the American Board of Ophthalmology. The father of this board was Edward Jackson; the mother was this Section, while the American Academy of Ophthalmology and Otolaryngology and the American Ophthalmological Society were foster parents. Jackson, in 1915, suggested such a board in a committee report to this Section, and through the joint action of the three societies the board was organized in 1916, with Jackson as chairman. For many years afterward W. H. Wilder was the prime factor in making the Board a success—in fact it became his "baby." If it is true that imitation is the highest compliment, then our Section has been complimented to an extreme degree, for most, if not all, the other specialties have since organized certification boards, albeit rather belatedly.

Being to a great extent hamstrung by the rules of the American Medical Association our Section, in comparison with independent societies, has been handicapped as regards setting of dues and assessments. However, as regards most other matters its progressive spirit has been unrestrained. Whenever a debatable question has arisen, our Section has pomptly appointed a committee to answer it. Only occasionally has a committee forgotten to bring in a report.

There is one way, however, in which our Section is a laggard, not as compared with other sections, but as compared with independent ophthalmologic societies. I refer to the failure to require certification by the American Board of Ophthalmology as a qualification for voting membership. I hope ours will take the lead over all other sections of the American Medical Association, as it has in so many other matters, in urging the powers that be to adopt such a requirement. This need not, in fact should not, bar any member of the American Medical Association from attending section meetings or from presenting a meritorious paper before any section.

The American Academy of Ophthalmology and Otolaryngology was organized in 1896 under the name of the Western Ophthalmic and Otolaryngologic Society, with Adolf Alt as the first president. In 1903 its name was changed to the present one. Its purpose was to serve the interests of men who combined all three specialties in their practices. This combination, obviously, was based on business reasons, not on similarities or overlapping fields, for ophthalmology is more closely related to neurology, or even to dermatology, than it is to otology or laryngology. At first the membership of the Academy consisted chiefly of midwesterners, but within recent years it has attracted to its fold most of the eastern ophthalmologists and now includes about all the eminent specialists in diseases of the eye, ear, nose and throat of the country. This may be partly because from the standpoint of scientific activities it really consists of two separate societies, which meet at the same time and place. The popularity of the Academy has been greatly enhanced by its instructional courses. So far as I know, it was the first medical society to institute such courses. Whenever I question a member returning from a meeting of the Academy, he always states that he gets more out of these meetings than out of those of any other society.

Another national society, the Association for Research in Ophthalmology, organized in 1929, perhaps before there was real need for it, is growing in importance and will no doubt soon firmly establish a unique place for itself, largely because it attracts and admits to membership investigation without medical degrees.

It is noteworthy that the first International Ophthalmological Congress, held in Brussels in 1857, antedated all national ophthalmologic societies. The representatives from the United States were Gross, Hays, Lazarus and Littell. The Congress has met in America only twice. In 1876 it was held in New York, and E. Williams, of Cincinnati, was elected president. In 1922 it was held in Washington, with de Schweinitz as president.

In addition to the national societies, fifteen sectional and numerous state and local ophthalmologic societies have sprung up all over the country and have contributed mightily to the progress of American ophthalmology. Time will not permit me to describe even those centered in New York, Philadelphia and Boston.

The following journals, now defunct, have played more or less important parts in the development of ophthalmology in this country: *American Journal of Ophthalmology* (1884-1917), *Ophthalmic Record* (1891-1917), *Annals of Ophthalmology* (1892-1917), *Ophthalmology* (1904-1916), *Ophthalmic Literature* (1911-1922) and *American Journal of Physiological Optics* (1920-1926). The *American Journal of Ophthalmology*, an entirely new journal, with an old name and with Edward Jackson as editor, took the place of the three journals discontinued in 1917.

Until within recent years, the ophthalmologist in this country either was largely self taught so far as his specialty was concerned or obtained his first special training abroad, notable in Vienna, Berlin or London. For years Vienna was the Mecca for American would-be ophthalmologists. Those who studied there could be divided into three classes; those who had failed to obtain an internship in America, those who sought the prestige connected with foreign study and, those who were chiefly motivated by the desire to obtain the best possible training. Those in the third class were fewest, but generally remained abroad the longest.

Until within about the past ten years, even the man who obtained an ophthalmic internship in this country was largely self taught. He was seldom taught anything by the staff of the hopsital or required to learn much. The internship, however, gave him an excellent opportunity to teach himself. I am inclined to believe that the self-taught ophthalmologist is the best taught provided his teacher has high intellectual qualifications and adequate clinical and laboratory facilities. As anticipated by its founders, the American Board of Ophthalmology has indirectly improved the teaching of ophthalmology by creating a demand ignorance of physiologic optics also still previls.

Forty years ago it was difficult to find a prominent American ophthalmologist, or even a professor of ophthalmology, who had any real knowledge of such basic subjects as physiologic optics or ophthalmic pathology. On the other hand, on the European Continent it was difficult to find any ophthalmologist who did not have such knowledge. I can recall that in those days, when an attempt was made to show almost any prominent American ophthalmologist a microscopic section, he would approach the microscope with his hands behind his back, displaying no desire to change the focus of the instrument or to adjust the slide. In fact, he would approach the instrument as though he feared it might bite him. You may expect me to say that conditions have now vastly changed, but I must disappoint you. American ophthalmologists sufficiently familiar with ophthalmic pathology to interpret or describe a microscopic section of a diseased eye are still extremely few. And almost equally as widespread ignorance of physiologic optics also still prevails.

During the past one hundred years the progress of ophthalmology has exceeded that within all previous centuries combined. Time will permit

me to mention only the outstanding achievements. The ophthalmoscope, perimeter, ophthalmometer, photometer, tonometer, electric magnet for removing foreign bodies, binocular corneal microscope, slit lamp and camera for fundus photography have been invented. Iridectomy, various filtration operations and cyclodialysis, for glaucoma, and operations for strabismus and for separation of the retina have been devised. The use of cocaine for local anesthesia, the prophylatic use of silver nitrate to prevent gonorrheal conjunctivitis in infants and the use of miotics to control glaucoma have been brought forward. Many diseases of the external and internal eye have been discovered, named and classified. Important discoveries relating to the normal and pathologic histology of the eye, and to the bacteriology of the eye have been made. Neuro-ophthalmology has been developed.

The sad fact must now be recorded that not one of these contributions, nor any other ophthalmologic contribution of fundamental importance, has originated in America. The ambition of American ophthalmologists has generally soared no higher than the attainment of the practical knowledge developed by their foreign colleagues. Nevertheless, American ophthalmologists have made to the advancement of their science many contributions of minor importance, and a few of considerable importance. Notable among the latter are Weeks's discovery of his bacillus (1886), Bail's report of the first case of conjunctivitis proved to be caused by Pasteurella tularensis (1914), Horner's discovery of a small muscle at the inner canthus (1824), Hasket Derby's discovery that mydriatics may precipitate an attack of glaucoma (1866), Holden's discovery of the cause of the red spot in the macula in amaurotic family idiocy (1898), Stevens' invention of the terms heterophoria, exophoria, etc. (1886), Duane's subjective parallax test for heterophoria (1889), Williams' corneal suture after cataract extraction (1886), H. B. Chandler's peripheral iridectomy (buttonhole) for cataract operations (1890), Wadsworth's slanted mirror for the ophthalmoscope (1877), Loring's ophthalmoscope with hinged mirror (1877), Dennett's electric ophthalmoscope (1885), Knapp's knife needle and his roller forceps, Hays's needle knife, Ziegler's knife needle, Noyes's scissors, Murdoch's speculum (1883) and Prince's advancement forceps. Also should be mentioned here the fact that Phillip Syng Physick was the first to suggest (1816) the use of absorbable sutures made of animal tissues. A notable American contribution to ophthalmology, although not by an ophthalmologist, was the invention of bifocal glasses in 1784 by Benjamin Franklin.

To name the bacillus discovered by Weeks the Koch-Weeks bacillus is unfair to Weeks. It is true that Koch had previously observed a similar bacillus in exudates from trachomatous eyes, but he had regarded it as a contaminating organism of no importance. Weeks, on the other hand, showed that his bacillus was the cause of a special form of conjunctivitis.

Henry W. Williams was the first to suture thewound after cataract extraction. He employed a single corneal suture, which he described in 1866; but, although he continued to advocate its use, it apparently was never adopted by any other surgeon. This may be because it had the serious fault of passing entirely through the cornea. However, sutures somewhat like that of Williams' are now coming into general use in cataract surgery.

Barraquer is generally given the credit for the method of removing the lens in capsule by the aid of a suction cup, although Hulen, of New York, described the method in 1910, seven years before Barraquer did so. However, this country cannot take credit for this operation, since essentially the same procedure was described by Stoewer in 1902. Nor can this country claim the operation now termed goniotomy. This has been perfected here but was devised by de Vicentiis in 1892. It was one of Haab's favorite operations for chronic glaucoma. He termed it anterior sclerotomy and in 1905 stated it was the best operation for infantile glaucoma. Vogt, in 1925, claimed the credit for originating the operation of cyclodiathermy. However, two Americans, in 1921, reduced intraocular pressure by applying destructive heat to the corneal limbus and therefore to the ciliary body.

According to the opinions of numerous American ophthalmologists who have visited foreign clinics, the best of our ophthalmic surgeons have been for many years more skilful than the best European surgeons. To explain this superiority, I assume that as a result of our diversity of population some of our surgeons have inherited an unusual degree of dexterity. On the other hand, a claim that our worst ophthalmic surgeons are the worst in the world might be difficult to refute.

Soon after the publication in 1866 of Donder's work on refraction, American ophthalmologists began to busy themselves with this subject, and by the end of the century had become expert in the determination of refractive errors. Following the lead of Weir Mitchell, a neurologist, many convinced themselves that uncorrected or improperly corrected refractive errors not only often caused headaches and ocular discomfort but caused or contributed to a variety of other symptoms, and even to organic disease. They did not devise any basically new methods of testing, but applied with meticulous care methods already known. It was believed that astigmatism of ⅛ D. could cause serious so-called eyestrain. Although severely exposed to this virus in my ophthalmologic infancy, I escaped infection. This may be because I was born in Kentucky, a state that borders on Missouri. The term eyestrain was undoubtedly invented in this country, but just when and by whom I do not know. If it has no other merit, it has that of satisfying patients. Their idea of what it means is indicated by such questions as, "Doctor do you find my eyes badly strained." I suspect that it was the overemphasis placed by

ophthalmologists on the importance of refractive errors that has led to the present unsatisfactory conditions relating to optometry. From what I have said, I hope no one will get the impression that I condone inaccurate refraction. In my own opinion, and in that of some of my patients, no one corrects refractive errors more precisely than I do.

Many excellent treatises dealing with ophthalmology have been published in this country. Among these may be mentioned textbooks by H. W. Williams,[6] 1862; by Noyes, [7] 1881, and 1890; by de Schweinitz,[8] 1892; by Weeks'[9] 1910; "Skiascopy, and Its Practical Application," by Edward Jackson, [10] 1895; "System of Diseases of the Eye," edited by Norris and Oliver,"[11] 1897-1900; "The American Encyclopedia and Dictionary of Ophthalmology," edited by Casey A. Wood,[12] 1913-1921; "The Eye and the Nervous System," edited by Posey and Spiller,[13] 1906. These books all served useful purposes in America, and some "filled a long-felt want," but it must be admitted that none of them quite reached the highest European standards.

In view of the great wealth of this country and the strong appeal made by blindness, it is remarkable how little has been donated to ophthalmic hospitals and for ophthalmic research. The Wilmer Institute, opened in 1924, and the Howe Laboratory of Ophthalmology, organized in 1931, were the first institutions in America especially endowed for ophthalmic research, and their endowments are still relatively inadequate. Now that government is preventing the accumulation of great private wealth, it may take over the financing of many institutions formerly largely dependent on private donations. That this is a desirable consummation is questionable.

During the past century this country has passed through five important wars, but separate ophthalmic departments in medical services were organized only in the two world wars. The ophthalmologists who manned these departments in each war were volunteers, not draftees. For the great sacrifices these men made, it cannot be said that on their return to civilian

7. Noyes, H. D.: A treatise [on] Diseases of the Eye, New York, W. Wood & Co., 1881; A Text-Book on Diseases of the Eye, ibid., 1890.

8. de Schweinitz, G. E.: Diseases of the Eye: A Handbook of Ophthalmic Practice, for Students and Practitioners, Philadelphia, W. B. Saunders Company, 1892.

9. Weeks, J. E.: A Treatise on Diseases of the Eye, Philadelphia, Lea & Febiger, 1910.

10. Jackson, E.: Skiascopy, and Its Practical Application to the Study of Refraction, Philadelphia, Edwards & Docher Co., 1895.

11. Norris, W. F., and Oliver, C. A.: System of Diseases of the Eye, Philadelphia, J. B. Lippincott Company, 1897-1898.

12. Wood, C. A.: The American Encyclopedia and Dictionary of Ophthalmology, Chicago, Cleveland Press, 1913-1917.

13. Posey, W. C., and Spiller, W. G.: The Eye and the Nervous System, Philadelphia, J. B. Lippincott Company, 1906.

life they were overwhelmed by the gratitude of those who had remained at home. A truthful account of the efficiencies and inefficiencies of the ophthalmic services in the two world wars would no doubt be of considerable interest, but is beyond the scope of this address, since these services contributed nothing of importance to the advancement of ophthalmic science, greatly as they contributed to the welfare of our armed forces.

However much it hurts our pride, the fact that this our country has been greatly excelled by other countries in contributions to ophthalmology would not be deplorable did it not mean neglect of superior opportunities. What is the cause of this deficiency? Long ago, two former chairmen of this Section attempted to answer this question. Harold Gifford, in his chairman's address in 1898, maintained that the answer lay in the meager qualifications required of medical teachers in this country. He said, "I think it is no exaggeration to say, leaving the smaller institutions out of the question, that in the best twenty of our medical schools more than one-half of the professors taken in the aggregate have received their positions for considerations which in Germany would hardly entitle them to the rank of privatdocent." In 1907 Alvan A. Hubbell wrote:

> "Physicians and surgeons have seldom been paid for teaching or for serving a hospital. The result has been, therefore, that without such a living salary as is paid to those attached to government schools and hospitals of Europe, our American medical teachers and hospital attendants have had to earn their living outside in private practice, and in doing this it has consumed nearly or quite all of their time and energy."

It seems to me that although what each of these astute ophthalmologists said is still true, there is a more fundamental cause of the deficiency in question. This is revealed by consideration of the fact that the deficiency is not confined to ophthalmology but exists throughout the whole of American science. For while America has excelled in the application of basic scientific facts, few of these facts have been discovered in this country. The explanation obviously lies in the lack of true scientific spirit. To a man imbued with this spirit, his discovery of a new fact is of itself sufficient reward without the addition of public acclaim or pecuniary return. It was natural that in the early days of this country paramount importance was given to the accumulation of tangible wealth, but the resulting attitude of mind persists here even today and continues to impede the development of the scientific spirit.

Now World War II has thrust on the United States leadership in ophthalmology, as in all other branches of medicine. At present this is a stimulus to the progress of ophthalmology here. It is to be hoped that, in spite of political obstacles which many of us fear we foresee in the near future, this accelerated progress will continue without interruption.

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ATROPHY OF THE OPTIC NERVE DUE TO MALNUTRITION

Report of two cases

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Two cases of atrophy of the optic nerve, probably due to malnutrition, are reported; this complication of malnutrition may be commoner now than the literature has indicated in the past. This greater frequency may be incident to the severe malnutrition to which some American prisoners of war were subjected. A short review of the available literature is given.

Lombroso (1869), Guaita, Rampoldi and several other Italian authors, as cited by Bietti,[1] reported atrophy of the optic nerve in pellagrins; but, as Bietti pointed out, other reasons for the atrophy had not been ruled out. The principal object of Bietti's report was an investigation of the relation of pellagra to retinitis pigmentosa. Microscopic examination of the eyes of 10 patients who had died of pellagra did not reveal a single case of atrophy of the optic nerve.

Whaley[2] reported on examinations of 36 pellagrins, 3 of whom had optic nerve atrophy; but, again, this may have been a coincidence, and the changes in the disk may have been due to other causes.

Calhoun[3] discussed the etiology of pellagra. In agreement with Goldberger, who had conducted a controlled dietary experiment at a penitentiary, he concluded that pellagra was of dietary origin. He also discussed the systemic and ocular symptoms. He reported on 10 patients with pellagra who were not alcoholic, did not smoke and were not addicted to the use of drugs. He accompanied the article with illustrations of their visual fields. The peripheral fields showed contraction for form and color; the central fields, absolute and relative scotomas for color. Examination of the fundus did not show hemorrhages but revealed temporal pallor and atrophy of the optic nerve in some patients.

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1. Bietti, A.: Ueber Augenveränderungen bei Pellagra, Klin. Monatsbl. f. Augenh. **39**:337, 1901.

2. Whaley, E. M.: Eye Symptoms of Pellagra, Tr. Nat. Conf. on Pellagra **1**:279, 1909.

3. Calhoun, F. P.: Alterations in the Visual Fields, associated with Pellagra, Am. J. Ophth. **1**:834 (Dec.) 1918.

In a discussion of beriberi, Elliot[4] summarized the ocular symptoms as those due to retrobulbar neuritis (central scotomas, diminution of central visual acuity and changes in the peripheral visual field); second, those due to paralyses of the muscles of the eye, including ptosis, and, third, decreased sensibility of the cornea. He pointed out that the fundus may present one of three appearances: no pathologic change, atrophy of the papillomacular bundle or atrophy of the whole disk. He reported that central vision hardly ever falls below 20/200. In his review of pellagra, Elliot mentioned the systemic and the ocular changes: asthenopia, circulatory changes in the retinal vessels, night blindness, amblyopia, atrophy of the optic nerve, cataract and pareses of the ocular muscles.

Cronin[5] reported a case of pellagra with ocular disturbance and phychosis in a patient 37 years old with chronic alcoholism. Vision was 20/200, not correctible, in the right eye and 20/20—2, corrected to 20/15, in the left eye. There was a central scotoma of the right eye, with no changes in the peripheral fields. Funduscopic study showed a macular hemorrhage and temporal pallor. On reexamination at a later date, vision proved to be nearly normal. Syphilis or multiple sclerosis was considered, but the anemia of pellagra was assigned as the most likely cause of the macular hemorrhage.

Levine[6] reported the case of a white woman aged 47, who was chronically alcoholic and exhibited all the cardinal symptoms and signs of pellagra, including greatly impaired vision, bilateral optic neuritis and cecocentral scotoma in both eyes. With a high protein diet and treatment with riboflavin, the patient made an excellent recovery. The author discussed the etiologic role of riboflavin, quoted J. H. Smith and pointed out the importance of an adequate sulfur intake (especially in the form of cystine) and normal sulfur metabolism as protection against solar radiation. He cited statistics showing the frequency of pellagra in the southern United States. He described the symptoms, pathologic features, treatment and prognosis of pellagra, with special attention to the ocular symptoms.

Carroll[7] reported on 10 patients, all chronically alcoholic and suffering from various degrees of visual impairment. Some patients had vision limited to counting fingers at 3 feet (90 cm.) and showed changes in the visual fields accordingly. These patients had pellagra or polyneuritis or both. When an antipellagra regimen was instituted, the patients showed

4. Elliot, R. H.: Tropical Ophthalmology, London, Oxford University Press, 1920.

5. Cronin, H. J.: Pellagra with Ocular Disturbances and Psyschosis, J. Nerv. & Ment. Dis. **78**:35 (July) 1933.

6. Levine, J.: Pellagra as a Cause of Optic Neuritis, Arch. Ophth. **12**:902 (Dec.) 1934.

7. Carroll, F. D.: "Alcohol" Amblyopia, Pellagra, Polyneuritis, Arch. Ophth. **16**:918 (Dec.) 1936.

striking improvement in visual acuity, visual fields and general condition, most of them regaining normal vision.

Fine and Lachman,[8] in an excellent article, reviewed the literature and reported on 3 patients, all alcoholic and pellagrous, who had impaired vision due to retrobulbar neuritis. In addition to the cutaneous and systemic symptoms, the patients showed impaired visual acuity, not correctible with glasses. With intensive vitamin therapy, the vision of 2 patients returned to normal and was greatly improved in the third. The fields showed chiefly central changes for white and colors; these also improved with therapy. Some patients exhibited temporal pallor of the disks. The relation of pellagra to polyneuritis, on the one hand, and to chronic alcoholism, on the other, was pointed out. Cowgill[9] and Jolliffe and associates[10] stated that the important etiologic factor is a deficiency in thiamine and riboflavin, the latter deficiency probably affecting the central nervous system. The 2 cases to be reported in this paper seem to offer evidence in favor of this hypothesis.

Beam[11] summarized the cases of 8 white men from 20 to 32 years of age. All these patients had been prisoners of the Japanese and had suffered from severe malnutrition during their confinement. They had received about 1,000 calories daily, with minimal amounts of protein and vitamins. These patients had a visual acuity of 1/200 to 10/200 in the better eye. All had bilateral central scotoma, and 2 patients showed concentric contraction of the fields. Funduscopic examination showed bilateral atrophy of the optic nerve. It is concluded that three etiologic factors may have been involved: a deficiency in vitamins, minerals and protein; intoxication of a chemical or bacterial nature, and the effect of strenuous physical work with inadequate caloric intake. He concluded, however, that the most important factor was a deficiency in thiamine.

REPORT OF CASES

CASE 1.—A white man aged 39 had been in perfect physical condition until about February 1942. In 1941 he was sent to the Philippines. At that time his vision was normal.

With the outbreak of the war, his food rations became very short. This poor diet apparently caused him to feel tired and weak for several weeks before his capture, on April 9, 1942. He was a prisoner of war until his liberation, in

8. Fine, M., and Lachman, G. S.: Retrobulbar Neuritis in Pellagra, Am. J. Ophth. **20**:708 (July) 1937.

9. Cowgill, G. R.: The Vitamin B Requirement of Man, New Haven, Conn., Yale University Press, 1934.

10. Jolliffe, N.; Colbert, C. N., and Joffe, P. M.: Observations on Etiologic Relationship of Vitamin B (B_1) to Polyneuritis in Alcohol Addict, Am. J. M. Sc. **191**:515 (April) 1936.

11. Beam, A. D.: Amblyopia Due to Dietary Deficiency, Arch. Ophth. **36**:113 (March) 1946.

February 1945. In May 1942 he seems to have had bacillary dysentery, causing severe weakness. This was treated successfully with sulfonamide drugs. In July 1942 he had jaundice and cystitis, lasting several months. The patient believes that in August 1942 he had "wet beriberi," characterized by edema of the face and severe pain with edema of the extremities. In August 1943 scurvy also developed, which was characterized by ulcers of the mouth and was improved by his eating a few limes. At the same time the patient apparently had pellagra, manifested by red, scaly, rough areas on the backs of his hands.

During July and August 1942 the patient noted a mild decrease in his visual acuity, the loss being equal in the two eyes. This became worse during September 1942, at which time he could see only the ground and moving objects, without being able to identify the latter. This severe impairment lasted until December 1942. The patient was transferred to a different camp in November 1942, and there the diet contained sufficient rice, vegetables and fruit. He was hospitalized but did not receive vitamin medication. He ascribes an improvement in his vision one month after his arrival in this new camp to the better diet.

In December 1942 the patient had his first attack of malaria; these attacks recurred monthly for the next ten months. Each attack was treated with quinine, which later was given prophylactically for many months. In April 1943 pronounced deafness developed. In August 1944 a diagnosis of dengue was made. From July 1944 on, the patient received intensive vitamin therapy and noted pronounced improvement in all his symptoms, although the caloric intake was less than before.

Shortly after the patient's liberation, in February 1945, the following diagnoses were made at an Army installation: malnutrition; beriberi; tinnitus aurium, and atrophy of the optic nerve, with vision of 20/400 bilaterally.

The patient was placed on a high caloric, high vitamin diet and was given high doses of preparations of vitamins A and D, ascorbic acid, riboflavin, nicotinic acid, thiamine and the vitamin B complex. Throughout this hospitalization he was given physical and occupational therapy. The blood counts were normal, and smears revealed no malarial organisms. The sedimentation rate was increased at first but became normal after several months. The urine and albumin-globulin ratio were normal, and cultures of the stools yielded no pathogens. The serologic reactions were negative. Electrocardiograms were normal. Roentgenologic examination of the chest showed no pathologic changes.

Reexamination about one year after his liberation showed notable improvement; use of the lower extremities, however, was still greatly impaired.

Ophthalmologic examination showed vision of 5/200 in each eye and bilateral atrophy of the optic nerve. A central scotoma was present in each eye.

When the patient was last examined, in December 1946, his general condition had further improved, but he was unable to get around without a cane.

Vision was 20/200 in the right eye and 10/400 in the left eye, not correctible in either eye. External examination of the eyes showed nothing unusual. Examination with the slit lamp revealed a small scar from a foreign body in each cornea. Funduscopic studies revealed nearly identical pictures in the two eyes: The disk was well outlined, with a small physiologic excavation; the temporal third of each disk was extremely pale with a greenish tinge; the lamina cribrosa was not seen; the blood vessels showed a slight increase in connective tissue for a distance of about ¼ disk diameter from the disk; adjacent to the temporal margin of the disk, there was an area of decreased retinal pigment, bordered temporally by a slight increase in pigment; the macula showed a central reflex and, like the rest of the fundus, showed no pathologic change.

The visual fields were difficult to take, since the patient was unable to fixate. For the peripheral fields, his forefinger was placed on the fixation point, and for the central fields, which were taken on the Lloyd stereocampimeter, he was instructed to look at the center of the circles. He was unable to see even the largest target in the center of the field.

The patient's peripheral fields, taken with a 4 mm. white target at 330 mm., showed slight contraction. The fields for blue and red were also slightly contracted and showed central scotomas, with a radius of somewhat less than 10 degrees and of identical size, for blue and red. Green was not recognized as such in any part of the field. Six targets were used on a 330 mm. perimeter. Bilateral central fields for 1 degree white showed a large cecocentral scotoma extending between 15 and 20 degrees in the upper field and to about 5 degrees in the lower field, these boundaries conforming to the path of the nerve fibers. All fields were taken with full illumination.

The ophthalmologic diagnosis was bilateral severe atrophy of the optic nerve; this was probably due to severe malnutrition and avitaminosis. The appearance of the disk suggested that the atrophy was preceded by optic neuritis.

CASE 2.—A white man aged 38 was well at the time of his capture on Bataan, on April 9, 1942. Early in 1942 his diet became poor and remained inadequate until his liberation, in September 1945. At the end of April 1942 he noted edema of the ankles, which disappeared during a severe attack of diarrhea early in May 1942. About the end of this month he had malaria, which was treated with quinine. Loss of weight at that time was about 55 pounds (24.9 Kg.). During July and August 1942 numbness of the toes developed, and during October 1942 he experienced pain in the toes, feet, ankles and legs up to the knese. At this time, also, there developed ulcers of the mouth and peeling of the skin of the scrotum. During the latter part of December 1942 the pain in the lower extremities became gradually worse, until it kept the patient awake at night. About January 5 or 6, 1943, vision failed suddenly and severely, the loss being about the same in the two eyes. The patient was transferred to a new camp, where the diet was much better for several months, and he gained 2 or 3 pounds (0.9 or 1.3 Kg.) a month. Several months after the improvement in his diet he noted that his vision gradually became better. This improvement lasted three months, after which his vision became somewhat worse again; this deterioration coincided with a change for the worse in his diet. From then on, his vision remained stationary.

The patient had a few more attacks of malaria between February 1943 and October 1944 and continued to show systemic signs of malnutrition, but there was no further deterioration in vision. He was liberated on Sept. 8, 1945. Thereafter, he received a high vitamin diet and regained the weight he had lost.

Physical examination on admission revealed nothing abnormal. The ophthalmologist stated in November 1945 that the patient showed partial atrophy of the optic nerve, secondary to retrobulbar neuritis caused by malnutrition. The patient received high vitamin medication and symptomatic therapy. Another ophthalmologic examination, three months later, revealed no change. A third examination of the eyes, about five months later, in July, 1946, showed vision of 20/100 in each eye, which was not correctible. External examination of the eyes showed nothing pathologic. Extraocular movements and pupillary reactions were normal. Funduscopic examination revealed a similar condition in the two eyes. The media were clear; the disk was well outlined and round, with a small physiologic excavation, and showed temporal pallor, the pale area involving the entire temporal half and having a greenish tinge; the blood vessels were normal; the macula showed no abnormality except for absence of the macular reflex; the retina was well pigmented,

and no other pathologic condition was seen. Examination with the slit lamp revealed nothing abnormal except for prominence of the corneal nerves and slight bulging of the right iris near the angle, in the 180 degree axis. The central fields showed bilateral absolute central scotoma nearly 2 degrees in size, which covered the fixation point. Temporal to the absolute scotoma, and continuous with it, was a sickle-shaped relative scotoma, extending another 2 degrees. Thus, it looked as though the central scotoma was reaching for the blindspot. The peripheral field was normal in both eyes.

To rule out retrobulbar neuritis with an etiologic basis other than malnutrition, the following work-up of the case was made: Otorhinolaryngologic examination showed no focus of infection; reactions to the test with purified protein derivative were negative after twenty-four and forty-eight hours; a consultant in genitourinary diseases found nothing abnormal; roentgenologic examination of all the teeth revealed no focus of infection; roentgenologic studies of the chest and paranasal sinuses and anteroposterior and lateral exposures of the skull showed no lesions; the spinal fluid was normal; agglutination tests gave negative reactions for typhoid, paratyphoid, undulant fever and Proteus vulgaris X19; repeated cultures of the stools yielded no pathogens; the serologic reactions were negative; the blood count and urine were normal, and special search for malarial parasites gave negative results.

A diagnosis of severe bilateral optic nerve atrophy was made; it was assumed that this was due to severe malnutriton and avitaminosis.

SUMMARY

The available literature on the relation between vitamin deficiences and optic nerve atrophy is briefly reviewed.

Two cases are presented. A detailed history is given in order to show that the visual difficulties were concurrent with other symptoms of vitamin deficiency and that the visual disturbances improved with an improvement in the diet.

No attempt is made to determine lack of which vitamin may have caused the atrophy of the optic nerve.

No attempt is made to determine whether the optic nerve atrophy was due to a primary disturbance in the ganglion cells of the retina, to optic neuritis or to retrobulbar neuritis.

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STUDIES IN EXPERIMENTAL OCULAR TUBERCULOSIS

X. The Effect of "Promin" and "Promizole" on Experimental Ocular Tuberculosis in the Immune-Allergic Rabbit

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The search for a chemical agent with a direct action on the tubercle bacillus began with the early observation of Koch that gold salts had an inhibitory action on the in vitro growth of the organism. Colloid of gold preparations were thereafter used clinically in the treatment of various tuberculous lesions, including laryngeal and ocular tuberculosis, and some encouraging results were reported. Untoward reactions, however, were so frequent, and sometimes of such severity, that in 1926 Calmette protested against the use of these preparations on the ground that the frequent deleterious effects greatly outweighed any favorable clinical action. Various dye preparations were later used in the treatment of ocular tuberculosis, but the reported results were not sufficiently encouraging to arouse any great enthusiasm for their use. In 1932 Wells [1] reviewed the literature on the chemotherapy of tuberculosis and concluded that of the many remedies proposed up to that time none had demonstrated the ability to arrest progress of a tuberculous infection either in man or in experimental animals. In recent years, however, the success achieved by various sulfonamide preparations in a wide variety of infections brought up the question of the possible use of some of these compounds in the treatment of tuberculosis. Interest in this possibility was especially stimulated by the report of Rich and Follis [2] in 1938. These authors reported

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This investigation was supported by a grant from the John and Mary R. Markle Foundation.

Read at the Eighty-Third Annual Meeting of the American Ophthalmological Society, Hot Springs, Va., June 7, 1947.

1. Wells, H. G.: The Chemotherapy of Tuberculosis, Yale J. Biol. & Med. **4:** 611 (March) 1932.

2. Rich, A. R., and Follis, R. H., Jr.: The Inhibitory Effect of Sulfanilamide on Development of Experimental Tuberculosis in the Guinea Pig, Bull. Johns Hopkins Hosp. **62:**77 (Jan.) 1938.

that treatment with sulfanilamide, begun prior to inoculation, had an inhibitory effect on the development of tuberculosis in the experimental guinea pig. However, the clinical use of sulfanilamide on various tuberculous infections failed to reveal any therapeutic action, and until the reports of Feldman and his co-workers no sulfonamide compounds were found with any direct chemotherapeutic action in tuberculosis.

In 1940 Feldman, Hinshaw and Moses[3] reported on the action of a sulfonamide preparation—the sodium salt of p, p′-diaminodiphenylsulfone- N, N′-didextrose sulfonate, known as "promin," on experimental tuberculosis in the guinea pig. After this preliminary paper, there appeared a series of reports from these investigators on experimental studies relating to the action of various sulfonamide preparations in tuberculosis. Three sulfones were found which had a definitely deterrent action on the progress of established tuberculosis in the experimental guinea pig. These preparations were "promin," "diasone" (disodium fomaldehyde sulfoxylate diaminodiphenylsulfone) and "promizole" (4, 2′-diaminophenyl-5′-thiazolylsulfone, an isomer of sulfathiazole). The deterrent action of these drugs is best illustrated by summarizing a few of the experimental reports of Feldman and his co-workers. In one report[4] on the action of promin, Feldman and his co-workers stated that when "promin" was given guinea pigs beginning either on the day of injection or three days or one, two, four or six weeks after the date of infection, it had a deterrent action on the ensuing tuberculosis; i.e., at the end of six months all control animals were dead, whereas 84 per cent of the treated animals were living. Of the living animals, 43 per cent showed no histologic lesions of tuberculosis, whereas 57 per cent showed lesions in the visceral organs or elsewhere. A suspension of the spleen of 8 of 17 treated animals failed to produce lesions on reinoculation. The "promin" was found to be more efficacious if given continually, although it still had a strong effect when given intermittently. In 1943 Feldman[5] and Hinshaw suggested that "promin" might have either a direct action against the tubercle bacillus or an indirect action in that the resistance of the host was made more effective by a degradation of the virulence of the infecting agent. In a later experiment,[6] however, he found no evi-

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3. Feldman, W. H.; Hinshaw, H. C., and Moses, H. E.: The Effect of Promin on Experimental Tuberculosis: Preliminary Report, Proc. Staff Meet., Mayo Clin. **15**:695 (Oct. 30) 1940.

4. Feldman, W. H.; Hinshaw, H. C., and Moses, H. E.: Promin in Experimental Tuberculosis, Am. Rev. Tuberc. **45**:303 (March) 1942.

5. Feldman, W. H., and Hinshaw, H. C.: Promin in Experimental Tuberculosis, Am. Rev. Tuberc. **48**:256 (Oct.) 1943.

6. Feldman, W. H., and Hinshaw, H. C.: Promin in Experimental Tuberculosis, Am. Rev. Tuberc. **51**:268 (March) 1945.

dence of an undue acquired resistance developing after treatment with "promin." The effect of "diasone"[7] was rather similar to that of "promin." Two hundred and eighty-eight days after treatment was terminated, 71 per cent of the control series were dead, whereas only 14 per cent of the treated group had died. He concluded that "diasone" likewise had a deterrent effect and that it was a little less toxic than "promin," although both drugs produced definite toxic symptoms.

"Promizole"[8] had a deterrent action similar to that of "promin," but was decidedly less toxic. In one experiment, treatment with "promin" and "promizole" was commenced in two series of guinea pigs prior to inoculation. The animals were then inoculated and the resulting disease was allowed to progress for sixty days, when the animals were killed. The degree of tuberculous infection was evaluated on a numerical scale.[9] The control group showed 66.4 per cent involvement, whereas the group treated with "promin" showed 4.4 per cent and the group treated with "promizole" 6.2 per cent involvement. In a second experiment, guinea pigs were inoculated, and the resulting tuberculosis was allowed to progress for periods of from six to ten weeks before treatment was started. At the end of two hundred and twenty-six days only 20 per cent of the control group survived, whereas 85 per cent of the group treated with "promin" and from 67 to 90 per cent of the group treated with "promizole" (depending on the time after infection that treatment was commenced) were still living. A histologic assay of the amount of tuberculosis in the survivors showed 83 per cent in the control group, 10.8 per cent in the group treated with "promin" and from 16.4 to 33.8 per cent in the various groups treated with "promizole." Suspensions of the spleens of 14 guinea pigs treated with "promizole" and injected into normal pigs were found to be infectious in only 4 animals. "Promizole" had a low toxicity and appeared to be an agent on the way to fulfilling the requirements of chemotherapeusis of tuberculosis.

Despite these highly encouraging experimental reports, which have been confirmed by other observers,[10] the clinical use of these compounds has in the main been disappointing. The present status has recently been

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7. Feldman, W. H.; Hinshaw, H. C., and Moses, H. E.: Therapeutic Effects of Disodium Formaldehyde Sulfoxylate Diaminodiphenylsulfone in Experimental Tuberculosis, Arch. Path. **36**:64 (July) 1943.

8. Feldman, W. H.; Hinshaw, H. C., and Mann, F. C.: Promizole in Tuberculosis, Am. Rev. Tuberc. **50**:418 (Nov.) 1944.

9. Feldman, W. H.: Scheme for the Numerical Recording of Tuberculous Changes in Experimentally Infected Guinea Pigs, Am. Rev. Tuberc. **48**:248 (Oct.) 1943.

10. Calloman, F. F. T.: New Derivatives of Diaminodiphenylsulfone, Am. Rev. Tuberc. **47**:97 (Jan.) 1943.

well summarized by Hinshaw, Feldman and Pfuetze.[11] A slight effect was obtained with "promin," but its toxicity limited its use. "Promizole" had an extremely low toxicity, patients receiving 12 to 16 Gm. per day with little or no reaction; but it had no effect on renal tuberculosis, failing to eradicate the bacilli from the urine of any of 10 patients for whom it was used. It had no effect in 5 patients with tuberculous meningitis or in 2 patients with miliary tuberculosis. Encouraging results were reported in cases of extrapulmonary infection, cutaneous tuberculosis, tuberculous lymphadenitis and tuberculous sinusitis. The reports on "diasone" were conflicting, Petter and Prenslau[12] obtaining encouraging results, whereas Pfuetze[13] found no convincing action. The drug was definitely toxic.

In their summary of the experimental and clinical results, Feldman and his co-workers stressed the need of more rapid methods of forecasting the chemotherapeutic possibilities of new compounds. They stated that in vitro studies were far from conclusive and that the experimental studies were open to the criticism that tuberculosis in the guinea pig is quite different from the disease in man.

In the light of the experimental results obtained by Feldman and his co-workers, it seemed worth while to study the effect of these sulfones on ocular tuberculosis. The reasons for such a study are twofold. First, the eye is a most favorable site for observing the chemotherapeutic effect of a drug; it permits accurate clinical observation and evaluation of the progress or regression of the disease during the period of treatment. Second, the clinical course of ocular tuberculosis in the immune-allergic rabbit is amazingly similar to the usual clinical pattern of the disease. Third, it is conceivable that a therapeutic effect may be more pronounced in a small, localized focus of tuberculosis, such as a lesion in the eye, walled off by the fibrous scleral envelope, than it would be in general systemic infection or in spreading lesions.

The use of "promin" in treatment of ocular tuberculosis has already been investigated by one group of authors, Steecken, Wolinsky and Heise.[14] These workers reported on the effect of "promin" treatment on ocular tuberculosis in the guinea pig and found that the intensity of the disease in the eye was definitely less in the treated animals than in the controls, but the results were not striking.

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11. Hinshaw, H. C.; Feldman, W. H., and Pfuetze, K. H.: Present Status of Chemotherapy in Tuberculosis, Ann. Int. Med. **22**:696 (May) 1945.

12. Petter, C. K., and Prenzlau, W. S.: Treatment of Tuberculosis with Diasone, Am. Rev. Tuberc. **49**:308 (April) 1944.

13. Pfuetze, K. H.: Diasone in Treatment of Pulmonary Tuberculosis, Dis. of Chest **11**:213 (June) 1945.

14. Steeken, W.; Wolinsky, E., and Heise, F. H.: Treatment of Experimental Ocular Tuberculosis with Promin, Am. Rev. Tuberc. **53**:175 (Feb.) 1946.

As part of the general study of experimental ocular tuberculosis, we have undertaken an evaluation of the action of some of the antibiotic and chemotherapeutic agents on ocular tuberculosis. In a previous paper [15] our experiences with penicillin were reported. In this study the therapeutic possibilities of penicillin were subjected to a severe test. Normal rabbits, in which ocular tuberculosis pursues a destructive course, were used. These rabbits were treated with immense doses of penicillin over a forty-five day period. No deterrent or antibiotic effect on the ocular tuberculosis was observed.

In the present study "promin" and "promizole" were used in treatment of immune-allergic rabbits. In such animals ocular tuberculosis runs a more restrained course than it does in the normal rabbit. In fact, the course of the disease and the various lesions of the cornea, iris and ciliary body are amazingly similar to the generally recognized clinical picture. The drugs were therefore subjected to a much less severe test than they would be if normal rabbits were used.

After the original systemic inoculation, in the groin with a virulent human strain, the rabbit exhibits an insignificant lesion at the site of inoculation. Thereafter a restrained systemic disease develops characterized usually by absence of macroscopic lesions, and only by microscopic miliary lesions in the liver and spleen in a limited number of the inoculated animals. Only occasionally does an individual rabbit die with widespread visceral or pulmonary tuberculous lesions. The disease tends to be self limited; the rabbits live indefinitely, but after about three months they acquire a definite hypersensitivity to tuberculin and an increased resistance to reinoculation. The latter is so great that it takes at least fifty times as great a dose of bacilli to produce ocular lesions in these animals as is required for the normal rabbit. After this immune-allergic state is established, the eyes are inoculated in the anterior chamber with a proper dose of the same strain of human bacilli. There then occurs in the eye an immediate inflammatory reaction to the tuberculin in the inoculum. This is dependent on the already established hypersensitivity, in which the eyes participate. This immediate reaction fades within a week, and then follows an incubation period of three to six weeks, dependent on the degree of immunity resulting from the systemic inoculation and the size of the inoculating dose of bacilli. The onset of the ocular disease is characterized by small, hard tubercles on the iris and in the cornea, with a moderate inflammatory reaction. This disease usually runs a restrained course; there is little acute inflammation, gross caseation or necrosis, and rarely, if ever, does the eyeball rupture. In three to six months the ocular

15. Kennedy, J. D.; Wood, A. C., and others: The Failure of Penicillin to Affect the Course of Experimental Ocular Tuberculosis, Arch. Ophth., to be published.

disease burns out, leaving inactive, but more or less scarred, eyes. The use of immune-allergic rabbits as test animals therefore provides a self-limited ocular disease of three to six months' duration, during which period the course and intensity of tuberculosis in the treated and untreated controls can be compared.

TECHNIC

The immune-allergic rabbits were prepared by injecting in the groin of normal rabbits 0.5 cc. of the paper filtrate of a six week old culture of virulent human tubercle bacilli. This inoculation was made in December 1945. By March 1946 a well marked cutaneous reaction to purified protein derivative had developed in all the rabbits. On May 13, they were inoculated in the anterior chamber of the right eye with 0.2 cc. of a paper filtrate of a six week old culture of the same organism, so diluted that it contained 25 to 50 organisms per oil immersion field. Within forty-eight hours these rabbits manifested the usual reaction to the tuberculin in the inoculum, which subsided within a few days. By June 24, 21 of the rabbits so inoculated showed early signs of ocular tuberculosis. They were then divided into three groups. Group 1, consisting of 6 rabbits, were untreated and served as controls. Group 2, consisting of 7 rabbits, were treated with "promin"; and group 3, consisting of 8 rabbits, were treated with "promizole." The treatment with both "promin" and "promizole" was commenced June 24 and was continued until the end of the experiment, in October.

The "promin" and "promizole" were given orally. The rabbits were fed with the usual "all-in-one" brand of rabbit pellets. The "promin" and "promizole" were sprayed over these pellets so that a 1 per cent concentration by weight of the drug was obtained in the food. A little "karo" syrup was added, and the pellets were dried. The rabbits were given all they could eat. Making allowances for wastage, it was calculated the individual rabbit consumed between 1,000 and 1,100 Gm. of this mixture a week, which gave an approximate daily dose of 1.5 Gm. of "promin" or "promizole" per rabbit per diem. This produced blood levels of from 1.5 to 3.7 mg. per hundred cubic centimeters. The concentration of the drugs in the aqueous was slightly less than one-third that in the blood.[16]

The rabbits fed "promin" lost on the average about one sixth of their body weight in the first four weeks, but thereafter their weight remained stationary. The rabbits fed "promizole" showed no untoward reaction to the drug.

All rabbits, both control and treated animals, were examined once a week, and the degree of clinical ocular tuberculosis was estimated on a numerical scale, in the manner described in the previous papers of this series. The average reading of each group was plotted each week on coordinate paper, to give a comparative graph of the course of the disease in the three groups.

In October 1946, when the period of observation was completed, the animals were killed and autopsied and the affected eyes removed. The eyes of one-half the rabbits in each group were sectioned for histologic study, and the eyes of the remaining rabbits were used for transmission experiments. Under aseptic precautions, these eyes were opened, and the uveal tract was removed and ground up in a sterile mortar with sand and a little saline solution. The supernatant extract was then inoculated into the anterior chamber of normal rabbits. These rabbits were kept under observation for three months for the development of clinical ocular tuberculosis. They were then killed and the eyes sectioned for study.

16. Determinations of the levels of "promin" and "promizole" in the blood and aqueous were made by Dr. E. K. Marshall.

RESULTS

Clinical Results.—The composite results are shown in figure 1, in which curve *A* represents the course of the untreated (control) rabbits, curve *B* the course of the animals treated with "promin" and curve *C* the course of the rabbits treated with "promizole." The initial peak in all the curves after inoculation represents the reaction to the tuberculin in the inoculum, which largely faded within the first week. Treatment was started at the beginning of the sixth week, when early tubercles were present in all the inoculated eyes. From the sixth to the ninth week, there was no evident difference between the course of the disease in the untreated controls and that in the treated animals. However, at the beginning of the ninth week after inoculation, and after three weeks of treatment, the course in the controls (group 1, curve *A*) and that in the

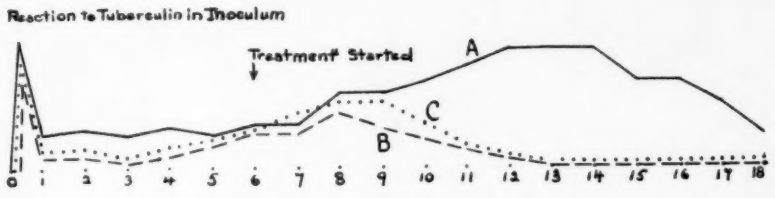

Fig. 1—Clinical course of ocular tuberculosis in immune-allergic control rabbits (curve *A*), immune-allergic rabbits treated with "promizole" (curve *B*) and immune-allergic rabbits treated with "promin" (curve *C*).

treated animals (groups 2 and 3, curves *B* and *C*) showed distinct differences. The tuberculosis in the control group slowly increased, with moderate inflammatory reaction, up to the twelfth week, when it reached an average maximum of 1.1. For the next two weeks the activity in the diseased eyes remained at the same level; beginning with the fourteenth week, it slowly declined, and at the end of the eighteenth week the average activity was rated as 0.3. At the end of the experiment, of the control group, 1 rabbit showed no activity, in 2 there was only a trace, in 2 the activity was estimated at 0.5 and the remaining rabbit still had fairly well developed ocular tuberculosis, estimated at 1.0.

After three weeks of treatment with "promin" and "promizole," the eyes of the treated rabbits began to improve slowly, and the curves for tuberculous disease in these groups began to separate from the curve for the control group. There was no appreciable difference in the curve for the group treated with "promin" and that for the group treated with "promizole." By the twelfth week, when the disease in the control group had reached its maximum, the ocular tuberculosis in the treated rabbits was almost completely inactive. At that time 1 of the 7 rabbits treated

with "promin" showed a maximum reaction of 0.5, while the disease in the remaining 6 animals was inactive and was rated at zero. Two rabbits of the 7 treated with "promizole" showed a faint trace of activity, and the disease of 5 was entirely inactive. At the end of the fourteenth week, when the activity in the controls was still at its maximum of 1.1, all the eyes of the rabbits treated with "promin" appeared entirely quiet, with

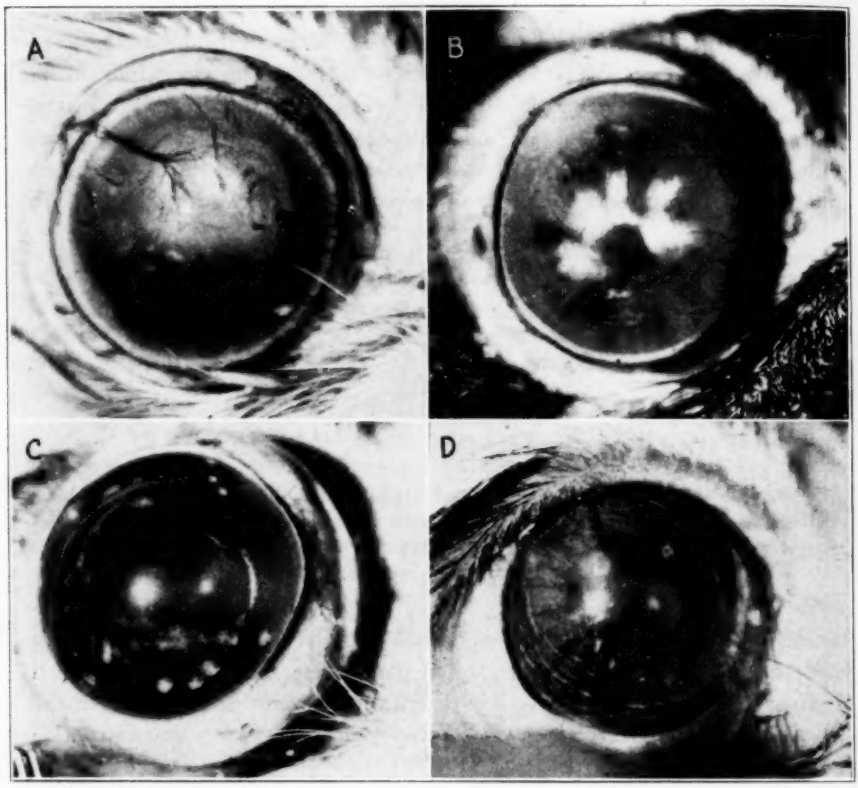

Fig. 2.—*A* and *B*, eyes of immune-allergic controls at end of the eighteenth week after inoculation, showing pericorneal congestion, infiltration of the cornea and corneal vascularization. Tubercles of the iris are still present.

C, eye of rabbit treated with "promin" at end of the eighteenth week, showing corneal scars and posterior synechiae. No activity is evident.

D, eye of rabbit treated with "promin" at end of the eighteenth week, showing an occasional circumscribed corneal scar and cicatrices of old tubercles in the iris. No activity is evident.

only slight residual scarring. At this time 1 of the rabbits treated with "promizole" still showed a trace of activity, while in 6 the disease was entirely quiescent. At the end of the sixteenth week all the treated eyes were entirely quiet, while 5 of the 6 control rabbits still showed active tuberculous disease of the eye, with an average activity of 0.8.

In figure 2 *A* and *B* is shown the clinical appearance of 2 of the control eyes at the end of the eighteenth week, illustrating the low grade pericorneal congestion, the corneal infiltration and the typical vascularization. Figures 2 *C* and *D* and 3*A* show the eyes of typical rabbits treated

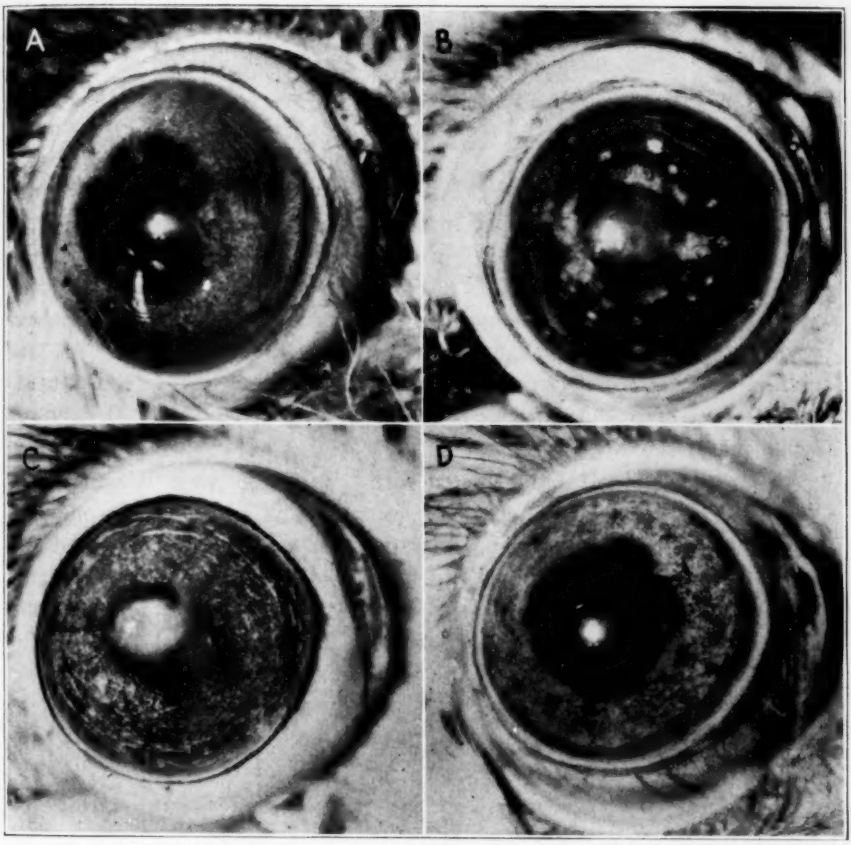

Fig. 3.—*A*, eye of rabbit treated with "promin" at end of the eighteenth week. The cornea is clear except for an occasional scar. There are posterior synechias and cicatrices of old tubercles in the iris, but no activity.

B, eye of rabbit treated with "promizole" at end of the eighteenth week, showing corneal scarring and posterior synechiae, but no activity.

C, rabbit treated with "promizole" at end of the eighteenth week, showing heavy central corneal scar and small cicatrices on the iris from old tubercles, with no activity.

D, rabbit treated with "promizole" at end of the eighteenth week, showing an entirely clear cornea (high light) and posterior synechiae in the iris, but no activity.

with "promin" at the end of the eighteenth week after inoculation. The eyes are white and free from inflammation. The corneas are clear except for the small, dense scars produced by the old lesions. The irises show some cicatricial scars and posterior synechias as residua of the former iritis, but there was no sign of any active inflammation. In figure 3*B*, *C*

and *D* are shown the eyes of typical rabbits treated with "promizole" at the end of the eighteenth week, presenting essentially the same picture as that of the rabbits treated with "promin," old scarring and no activity.

Histologic Results.—Three eyes of the control rabbits (group 1) were sectioned for study. All showed roughly the same histologic picture of numerous tubercles scattered throughout the cornea, iris and ciliary body, with little or no caseation or necrosis. Figures 4, 5 and 6 show the typical tuberculous lesions observed in an untreated immune-allergic rabbit with still active ocular tuberculosis. Figures 4 and 5 show a rather large tubercle in the cornea with epithelioid cells, giant cells and lymphocytes, but with the usual conspicuous absence of caseation. Figure 6 shows a small tubercle on the surface of the iris.

Of the rabbits treated with "promin" (group 2), the eyes of 4 were sectioned for histologic study. Two of these eyes showed no lesions of any sort other than moderate scarring of the iris (fig. 7). One eye showed several small tubercles in the iris but no other lesions (fig. 8). The remaining eye showed only one lesion in the sections studied—a small, healing lesion in the cornea, little more than a residual collection of lymphocytes (fig. 9).

Four eyes of the rabbits treated with "promizole" were sectioned and studied. One eye showed no active lesion of any sort. The second eye showed two minor foci, one a healed lesion in the cornea (fig. 10) and one an old, hard tubercle in the iris (fig. 11). The third eye presented several old healing and healed tubercles in the ciliary body (fig. 12), while the last eye showed scarring and thickening of the iris (fig. 13) and an old healed tubercle in the cornea (fig. 14). Thus, there was a definite contrast between the eyes of the control and those of the treated rabbits. In general, the controls showed many more lesions, which were larger and more active than the few lesions observed in the treated animals.

Transmission Experiments.—In the control group, the uveal tracts of 3 eyes were ground up for inoculation into the eyes of normal rabbits. All 3 transfers produced the disease, and the inoculated rabbits presented the classic picture of ocular tuberculosis in the normal rabbit, the first tubercles appearing about two weeks after inoculation and the eyes progressing to rupture by the twelfth week. Figure 15 shows the disease in 1 of these eyes at the end of the tenth week, with advanced tuberculosis of the uvea, heavy corneal infiltration and vascularization. Figure 16 presents another of these eyes, with a similar picture and beginning corneal ectasia. The histologic picture in the eyes of these transfer rabbits is illustrated in figure 17, showing a ruptured globe, and in figure 18, showing the advanced, caseating lesions of the cornea and ciliary body. These pictures, both clinical and histologic, are in sharp contrast with *A* and *B* of figure 2, which illustrate the clinical picture, and with figures 4, 5 and 6, which

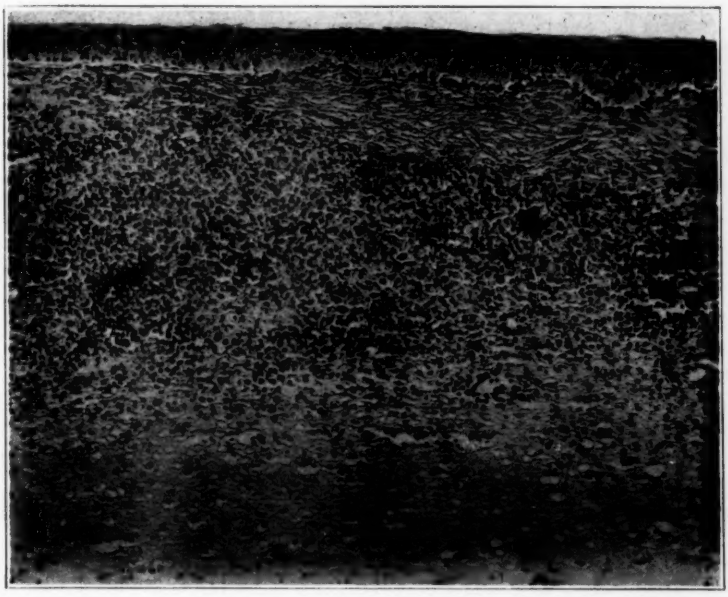

Fig. 4.—Tubercle in the cornea of an untreated immune-allergic rabbit; × 100.

Fig. 5.—Tubercle in the iris of an untreated immune-allergic rabbit; × 100.

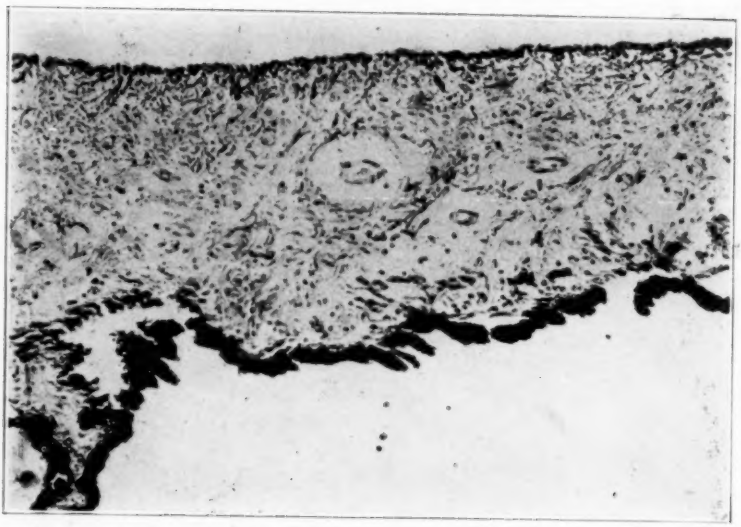

Fig. 6.—Tubercles at the root of the iris and in the ciliary body of an untreated immune-allergic rabbit; × 100.

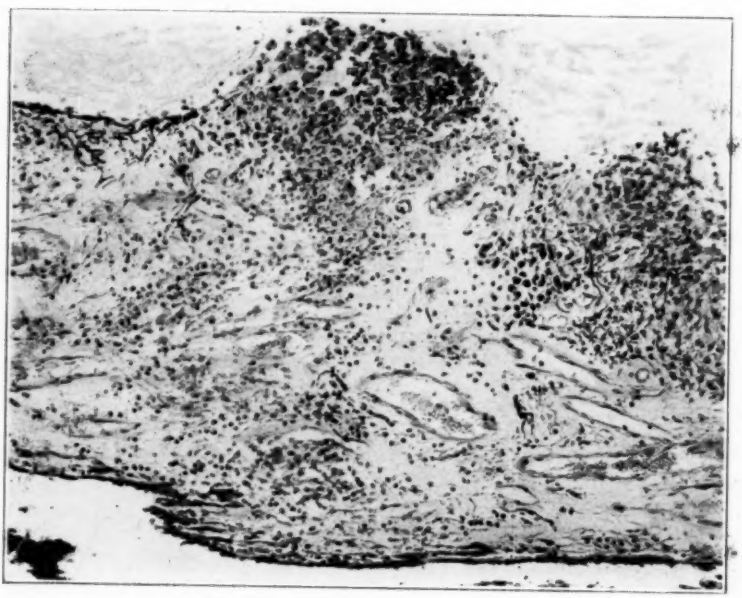

Fig. 7.—Iris of an immune-allergic rabbit treated with "promin"; × 100.

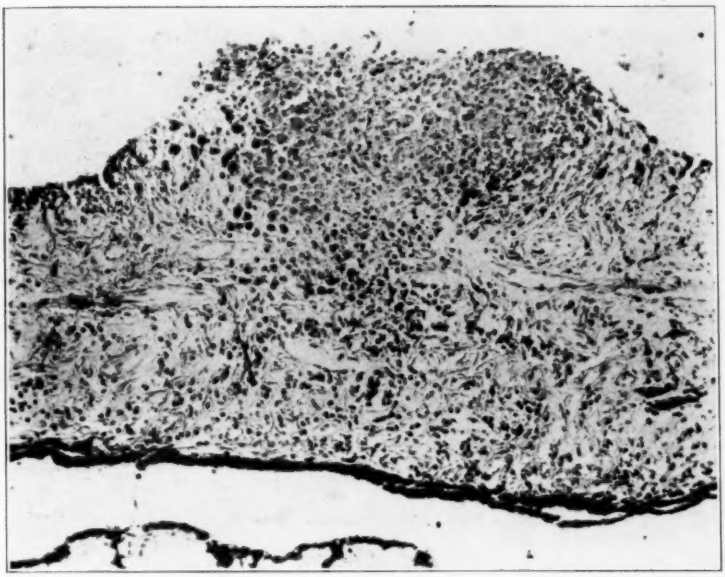

Fig. 8.—Small tubercle on the iris of an immune-allergic rabbit treated with "promin"; × 100.

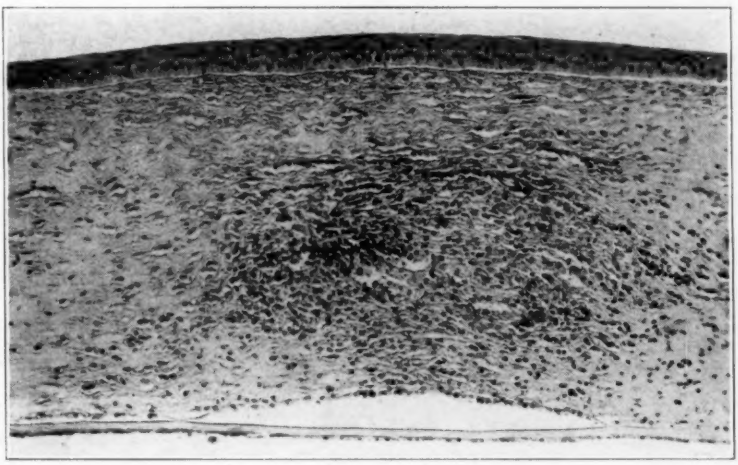

Fig. 9.—Tubercle of the cornea of an immune-allergic rabbit treated with "promin"; × 100.

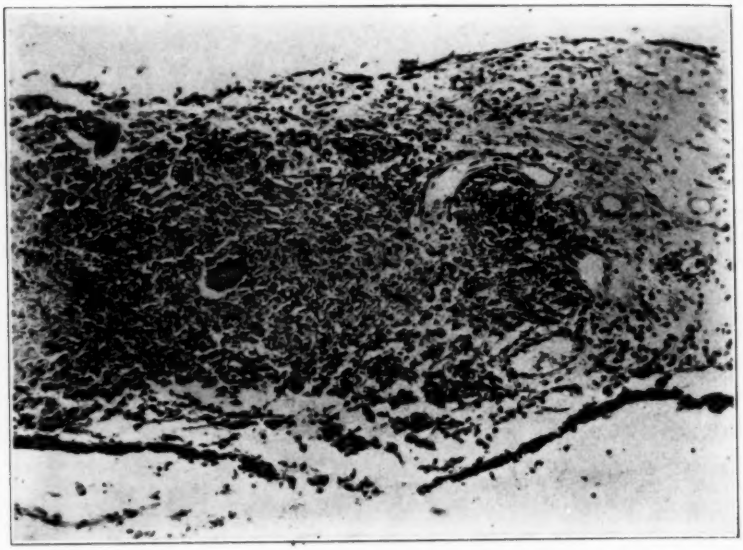

Fig. 10.—Healed tubercle on the cornea of an immune-allergic rabbit treated with "promizole"; × 100.

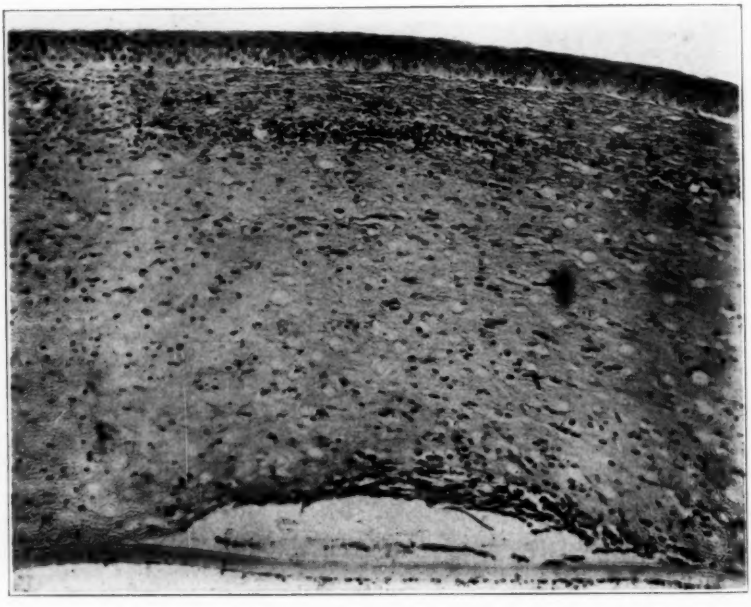

Fig. 11.—Tubercles in the iris of an immune-allergic rabbit treated with "promizole"; × 100.

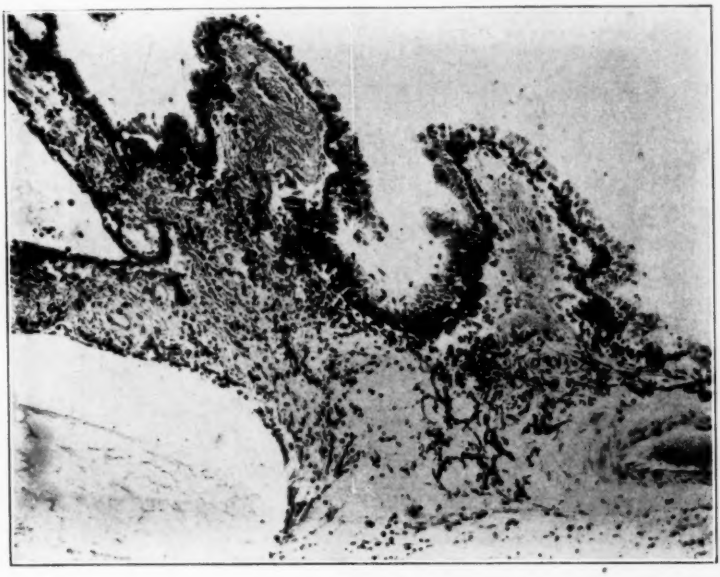

Fig. 12.—Encapsulated tubercle of the ciliary body of an immune-allergic rabbit treated with "promizole"; × 100.

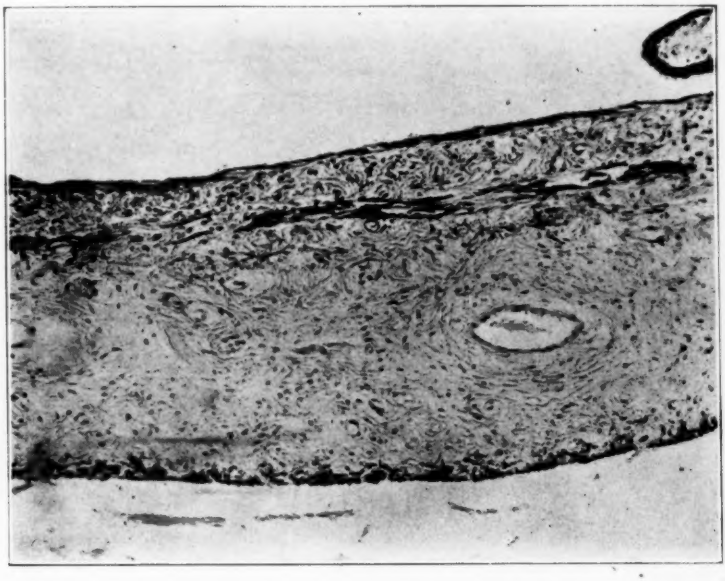

Fig. 13.—Scarring of the iris in an immune-allergic rabbit treated with "promizole"; × 100.

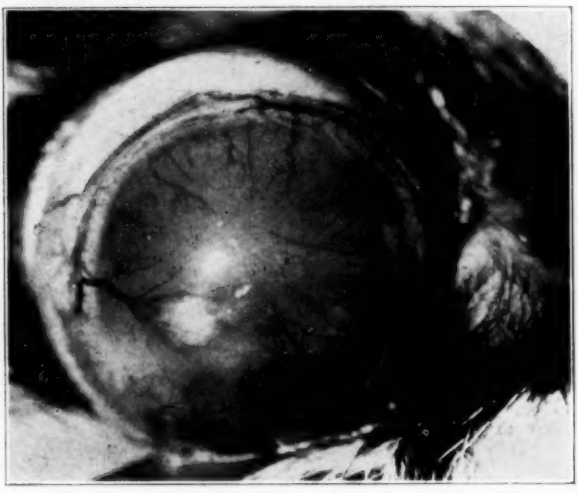

Fig. 14.—Healed tubercle of the cornea in an immune-allergic rabbit treated with "promizole"; × 100.

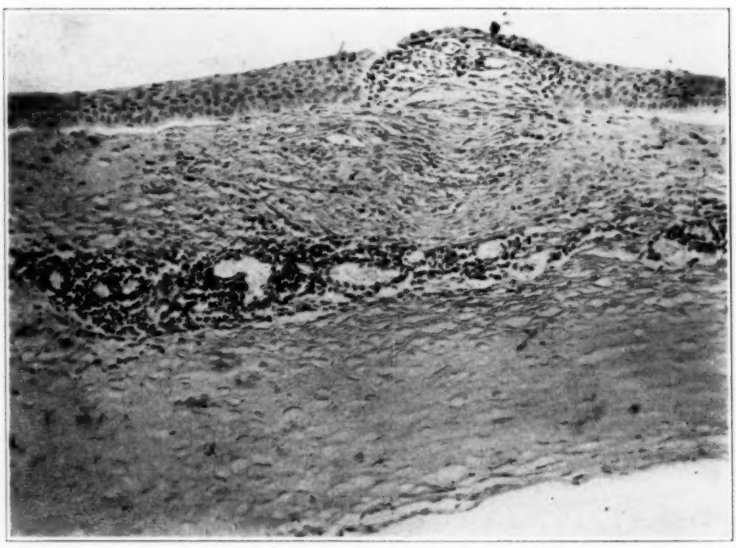

Fig. 15.—Clinical appearance of a normal transfer rabbit, illustrating advanced spreading corneal infiltration blocking all view of the iris.

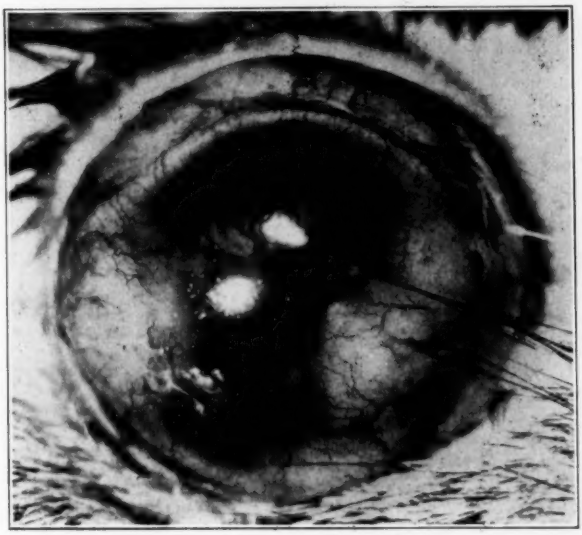

Fig. 16.—Clinical appearance of a normal transfer rabbit, illustrating violent inflammatory reaction, corneal infiltration and beginning necrosis and ectasia of the cornea.

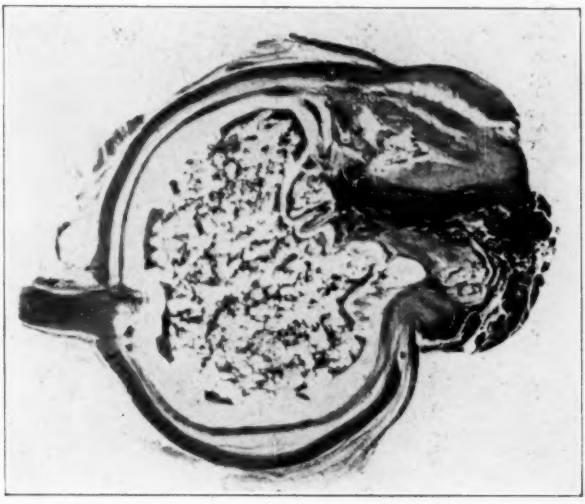

Fig. 17.—Ruptured globe following inoculation of a normal eye by transfer from an immune-allergic control; × 100.

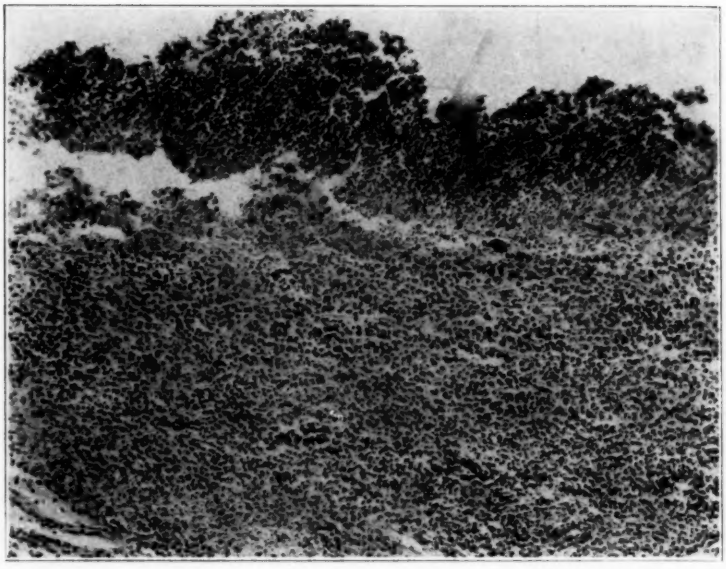

Fig. 18.—Multiple tubercles of the cornea with caseation in the cornea of a normal rabbit inoculated by transfer from an untreated immune-allergic control; × 100.

Fig. 19.—Ciliary region of a normal rabbit eye inoculated by transfer from an untreated immune-allergic control; × 100.

illustrate the histologic lesions, in the immune-allergic rabbit. They present clearly the radically different courses of ocular tuberculosis in the normal and in the immune rabbit.

Three eyes of the rabbits treated with "promin" were used for transmission studies. At the end of three months, the result of 1 of the transfers was positive and the results of 2 were negative. In the rabbit with the positive transfer there developed tubercles on the iris and infiltration and vascularization of the cornea after the long incubation period of two months, indicating that the organisms in the inoculating dose must have been either extremely scanty or of attenuated virulence. These eyes were then sectioned, and the two clinically nontuberculous eyes were likewise observed to be entirely normal on histologic study. The histologic picture of the sectioned eye of the rabbit with the positive transfer was similar to that in the eyes of the control transfer rabbits.

The extract of the uveal tract of 4 of the rabbits treated with "promizole" was injected into the anterior chambers of the eyes of normal rabbits. One of the transfer rabbits acquired a secondary infection and was discarded. At the end of three months the eyes of the remaining 3 transfer rabbits were entirely negative for tuberculosis. The animals were then killed and the inoculated eyes removed and sectioned. These eyes all showd no histologic evidence of tuberculosis.

In summary, all the eyes of the control rabbits produced tuberculous lesions on transfer. The eyes of 1 of 3 rabbits treated with "promin" produced tuberculosis on inoculation, and those of 2 did not. Three eyes of the rabbits treated with "promizole" did not produce tuberculous lesions on transfer, an additional eye being discarded on account of secondary infection.

COMMENT

These results require little comment. It is evident that both "promin" and "promizole" have a deterrent action on the course of ocular tuberculosis in the immune-allergic rabbit. Clinically, this deterrent action began to be manifest after three weeks of treatment, and by the fourteenth week the disease was under control and entirely quiet in the eyes of 14 of 15 treated rabbits, while the eye of the fifteenth rabbit showed only a trace of activity. The therapeutic effects of "promin" and "promizole" appeared to be about the same. "Promizole" did not produce any toxic symptoms, while some of the rabbits treated with "promin" perceptibly lost body weight. Neither "promin" nor "promizole," however, appeared to effect a complete cure of the ocular tuberculosis. Of the 7 eyes of treated rabbits sectioned for study, 5 still showed definite tuberculous lesions, although the lesions were much fewer and less severe than those shown by the eyes of the control animals. It is quite possible, even probable, that had complete serial sections been made of the 3 eyes apparently showing no

tuberculous lesions, small lesions would have been observed in these eyes.

The results of the transmission experiment likewise illustrate the deterrent action of "promin" and "promizole." Whereas all the control transfer eyes produced tuberculous lesions on inoculation, only 1 of the treated transfer eyes was infective. There is nothing in this experiment that throws any light on how this lack of infectiousness was attained, whether by a bactericidal effect of the drugs on the bacteria or by an attenuation of the virulence of the organisms, allowing the preexisting immunity to become more effective.

It should be emphasized that so far this deterrent action of "promin" and "promizole" on ocular tuberculosis has been demonstrated only in the immune-allergic rabbit, in which, in addition to the chemotherapeutic effect of these sulfones, a fairly high degree of systemic immunity was also induced by the preceding systemic injection. It should be remembered that Feldman has already suggested that these sulfones may owe their deterrent action to a degradation of the virulence of the invading organisms, thus rendering the resistance of the host more effective. He did not find any evidence of increased acquired resistance developing after treatment with sulfone. In line with this suggestion, it will be interesting to see whether any deterrent action of "promin" or "promizole" against ocular tuberculosis can be demonstrated in the normal rabbit. Certainly, in this study the results may be due either to an attenuation or degradation in the virulence of the invading organism or to a specific chemotherapeutic bactericidal action.

SUMMARY AND CONCLUSIONS

1. Both "promin" and "promizole" exert a deterrent action on the course of ocular tuberculosis in the immune-allergic rabbit. This deterrent action becomes evident after the third week of treatment. This action of the two drugs is about the same.

2. Histologic evidences of tuberculous disease persist in the majority of the eyes of the treated animals. The lesions, however, are fewer and are less severe than in the control eyes.

3. In transfer experiments with the extract of the uveal tract from the eyes of the 7 treated animals, only 1 positive result was obtained. This occurred only after an incubation period of two months. All the control eyes gave positive transfers.

4. These results may be due either to a degradation or an attenuation of the virulence of the organisms, allowing the resistance of the host to become more effective, or to a direct bactericidal action on the bacilli.

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DACRYOCYSTITIS OF INFANCY

A Review of One Hundred Cases

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In the management of dacryocystitis of infancy both pediatricians and ophthalmologists have as a rule recommended conservative treatment. The teaching has been that no attempt should be made to open the nasolacrimal passages by probing the duct because early instrumentation would injure the tissues and interfere with their normal evolution. This seemed reasonable; hence, conservative treatment has been followed with but few exceptions. From a review of the literature and the present series of cases, it seems that passive treatment may at times be more harmful than early probing of the duct.

REVIEW OF LITERATURE

There were innumerable articles during the past century warning against probing the nasolacrimal duct in cases of dacryocystitis in infancy. In 1904 Weeks [1] proposed probing the duct with a fairly large probe after slitting the canaliculus provided that conservative treatment was unsuccessful and nature had been given every opportunity to establish a passage. Pechin,[2] in 1905, in discussing dacryocystitis of infancy, expressed the opinion that it might be due to meconium in the nose which blocked the lower end of the nasolacrimal duct and that its expulsion would result in a cure. Cosmettatos,[3] in 1906, described five congenital anomalies of the lacrimal passages: a lacrimal cleft instead of a punctum, an extra lacrimal canal, an undeveloped lower canaliculus, absence of the lower punctum and a congenital fistula of the lacrimal sac. Zentmayer,[4] in 1907, advocated early dilation of the duct with probes if conservative

1. Weeks, J. E.: Congenital Occlusion of the Lacrymal Canal and Acute Contagious Inflammations of the Conjunctiva in Children, J. A. M. A. **43**:1760 (Dec. 10) 1904.

2. Pechin: Dacryocystite congénitale atténuée: pseudo-conjonctivite des nouveaunés d'origine lacrymale, Arch. d'opht. **25**:490, 1905.

3. Cosmettatos, G. F.: Ueber einige angeborene Anomalien der Thränenwege, Arch. f. Augenh. **55**:362, 1906.

4. Zentmayer, W.: Congenital Dacryocystitis, Pennsylvania M. J. **11**:895, 1907.

treatment was not successful. Two discussants (J. Ferdinand Klinedinst and W. Campbell Posey) of Zentmayer's paper described such radical treatment as likely to do permanent damage by tearing or overstretching the lacrimal canal.

Edward Jackson,[5] in 1907, pointed out that the lacrimal secretion does not appear for several weeks after birth and that the lacrimal passages during this time may not be patulous. Since no functional call is made on the lacrimal passages, no symptoms are noted provided the opening occurs in time for the demands on it. If infection occurs, the symptoms start.

> It should be remembered that the development of the lacrimal duct is a process of physiologic development and is likely to be completed at any time. We should await its completion, meanwhile controlling the inflammatory process as well as possible by palliative treatment. Conservative treatment should not be limited to a period of two to six months but as long as the symptoms are controlled by such treatment.[5]

Ollendorf,[6] in 1907, reported 7 cases of dacryocystitis of infancy in which he had been unsuccessful with conservative treatment but in which the condition promptly cleared after the duct had been probed. In 1908 Zentmayer[7] discussed the embryology of the nasolacrimal duct: how it arises as a thickening of epidermis along the line of the nasolacrimal groove, forming at first a ridge and later a solid cord. The cord is converted into a canal by the separation of epithelial cells. This debris of cells fills the canal with a gelatinous mass until the seventh fetal month or later. He cited possible causes of dacryocystitis of the newborn, such as (1) delayed necrosis of the cells forming the cord, (2) retention of the separated cells in the lower end of the duct, (3) obstruction due to folds of the mucous membrane in the duct and (4) partial occlusion from pressure of the turbinate bones. Zentmayer advocated probing and found that one such treatment was usually sufficient.

Kraupa,[8] in 1910, reported an instance of absence of the lacrimal puncta in a 14 year old boy. One eye showed complete absence of the puncta of the upper and lower lids, while the other eye showed absence of the upper lacrimal punctum.

The most valuable description of the genesis and development of the nasolacrimal passages was published in 1912 by Schaeffer.[9] This study

5. Jackson, E.: Delayed Development of the Lacrimal-Nasal Duct, Ophth. Rec. **16**:321, 1907.

6. Ollendorff: Die Tränensackeiterung der Neugeborenen, Ophth. Klin. **11**:47, 1907.

7. Zentmayer, W.: Imperforation of the Lachrymonasal Duct in the Newborn, and Its Clinical Manifestations, J. A. M. A. **51**:188 (July 18) 1908.

8. Kraupa, E.: Die angeborene Atresie der Tränenröhrchen und ihre operative Behandlung, Klin. Monatsbl. f. Augenh **48**:445, 1910.

9. Schaeffer, J. P.: The Genesis and Development of the Nasolacrimal Passages in Man, Am. J. Anat. **13**:1, 1912.

was made on a series of specimens representing stages from 30 day embryos to full term fetuses.

> The nasolacrimal duct starts from a thickening of epidermal cells in the twelve millimeter embryo which grows down into the mesenchymal tissue and detaches itself from the surface ectoderm. This epithelial cord begins to develop some lumen by the third month. Sections through one hundred day embryos show that the superior and inferior canalicular cords have extended to the free border of the eyelids and that the nasal end of the mother cord of cells has reached the nasal mucous membrane. Irregular lumens are present at various parts of the cords, more toward its extremities than at its center. The ocular end establishes a lumen long before the nasal end and the latter is delayed approximately until birth or a little later. The last portion to become patent is the site of coalescence between the nasal sprout of the mother cord and the nasal mucous membrane. The position of the ostium whether at the highest point of the inferior meatus or at some lower site on the lateral nasal wall and the shape of the ostia whether large, wide open, or more or less guarded by folds of mucosa depends upon the point and extent of coalescence between the nasal end of the mother cord and nasal mucosa.[9]

This exhaustive description of the genesis of the nasolacrimal duct is replete with illustrations of imperforate ducts in both 7 month and full term fetuses.

Wiener and Sauer,[10] in 1914, reported 2 cases in persons 50 and 70 years of age, respectively, in which an imperforate membrane obstructed the lower end of the lacrimal duct. A probe passed through the duct was located in the inferior meatus under the mucosa, and it was necessary to have the mucosa slit over the probe to establish the patency of the nasolacrimal membrane. In 1917, Roy,[11] in reporting on a questionnaire sent to a number of ophthalmologists asking their treatment of epiphora of the newborn, found that most of the replies favored conservative management, in the belief that the ailment commonly corrected itself with the development of the child. He advocated massage of the lacrimal sac together with use of an astringent wash for the eye, and also cleaning the nasal cavity as a routine.

Green,[12] in 1917, said that infantile dacryocystitis was the result of blockage of the lower end of the duct with fetal remains. He asked:

> What do we do if we are dealing with a hypodermic needle that has become plugged with dirt, cotton, or dried blood? We push the plugs through with a fine wire. In probing an infant's lacrimal duct we are establishing a normal function with less danger to the tissues than treatment by forceful pressure over an infant's tear sac that has laready been weakened by distention and infection.

He reported 3 cases in which the condition cleared up with one probing.

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10. Wiener, M., and Sauer, W. E.: Dacryocystitis Caused by a Membranous Closure of the Nasal Duct, Ann. Ophth. **23**:487, 1914.

11. Roy, D.: Lacrymal Stenosis in Infants and Its Treatment, Charlotte M. J. **75**:78, 1917.

12. Green, J.: Treatment of Dacryocystitis in Infants, J. Missouri M. A. **14**: 427, 1917.

Curdy, in discussing Green's paper, objected to probing as likely to prevent the normal development of the duct. Fuchs,[13] in 1917, said:

> The upper end of the canal is the narrowest part of the duct; there is a venous plexus surrounding the nasolacrimal duct. The mucosa of the duct and sac is lined with a double layer of cylindrical epithelium. Mucous membrane projects in folds into the lumen of the lacrimal passages (called valves).

In Cunningham's "Anatomy,"[14] the nasolacrimal duct is described as about 18 mm. in length, with a diameter of 3 or 4 mm., the duct being directed downward and slightly backward. It opens at the junction of the anterior one fourth with the posterior three fourths of the inferior meatus of the nose.

Schaeffer,[15] in 1920, described as very common, irregularities and diverticula of the nasolacrimal duct, with an occasional side to side union of the lacrimal sac and the nasolacrimal duct. Successful probing of the duct depends on a lacrimal sac merging gradually with a nasolacrimal duct, with a fairly regular contour; otherwise artificial openings and passageways may occur with probing. He described and illustrated eleven types of nasolacrimal ostiums and stated:

> . . . the abutting layers of epithelium with a limited amount of intervening connective tissue may not rupture at birth or shortly after. Atresia in the newborn is due to an unruptured lacrimonasal membrane, and in these surgical intervention may be necessary.[15]

Nagel,[16] in 1920, finding only one reference to bilateral congenital atresia of the nasolacrimal duct in the literature up to that time, stated that it was rare. He advocated conservative treatment and, if this failed, probing through the upper canaliculus into the duct. McMurray,[17] in 1921, reported on 2 children with congenital stenosis of the nasolacrimal duct whom he treated conservatively until he considered them old enough to have the nasolacrimal ducts dilated safely (from 3 weeks until 2½ years of age). The treatment was expression of the sac, with the instillation of mild protein silver U.S.P. Stieren and Krebs, in discussing McMurray's paper, advocated probing the duct with the patient under general anesthesia if the conservative treatment was not successful within three or four weeks. Van der Hoeve,[18] in 1921, pointed out that amniotic

13. Fuchs, H.: Text-Book of Ophthalmology, edited by A. Duane, ed. 8, Philadelphia, J. B. Lippincott Company, 1917.

14. Cunningham, D. J.: Cunningham's Manual of Practical Anatomy, ed. 5, New York, William Wood & Company, 1921, p. 825.

15. Schaeffer, J. P.: The Nasolacrimal Passageways, in The Nose and Olfactory Organ in Man, Philadelphia, P. Blakiston's Son & Co., 1920, p. 244.

16. Nagel, C. S. G.: Congenital Atresia of the Lacrimal Duct,, Am. J. Ophth. **3**:406, 1920.

17. McMurray, J. B.: Congenital Stenosis of Nasolacrimal Duct, Pennsylvania M. J. **25**:494, 1921.

18. van der Hoeve, J.: The Development of the Lacrymal Canal in Normal and Abnormal Conditions, Tr. Coll. Physicians, Philadelphia **43**:187, 1921.

bands may form barriers to the development of the lacrimal caruncle and ducts. In 1921 Zentmayer [19] noted that 25 per cent of cases of dacryocystitis occurred before the tenth year and that the condition was due to an inadequately treated congenital atresia.

Kramer,[20] in 1922, tried to associate the etiologic factor in congenital dacryocystitis with gonorrhea in the parents. Doub and Carter,[21] in 1922, visualized the nasolacrimal passages roentgenographically in adults but not in children. In 1923 Crigler [22] advocated manual expression with pressure exerted by the thumb over the sac to force an obstructing plug from the unopened end of the duct. Meller,[23] 1923, advocated conservative management, but if this failed, he recommended probing of the duct, preferably with a hollow probe to which a lacrimal syringe could be attached to avoid the inconvenience of having to irrigate the sac and duct. Peters,[24] in 1923, in a report of cases in two families, expressed the opinion that congenital atresia of the nasolacrimal duct might be hereditary and familial.

Rollet,[25] in 1927, stated the opinion that treatment of congenital dacryocystitis should consist of irrigations and expression of the sac, and not of instrumentation. Arrand, in a discussion of Rollett's paper, advocated forceful irrigation of the lacrimal passages by catheterization of the duct. Coronat further observed an abscess of the sac after catheterization. Lyle,[26] in 1928, compared roentgenographically the nasolacrimal duct of infancy with that of an adult. Campbell and Carter,[27] in 1929, pointed out that "any treatment of lacrimal stenosis to be thoroughly effective, must relieve the collection of tears and pus in the patient's eyes." Meller,[28] in 1929, advocated expression of the sac and, if this failed, probing of

19. Zentmayer, W.: Congenital Atresia of the Lacrimonasal Duct, Tr. Coll. Physicians, Philadelphia **43**:172, 1921.

20. Kramer, R.: Zur Ätiologie der Dacryocystitis congenita, Ztschr. f. Augenh. **49**:20, 1922.

21. Doub, H. P., and Carter, J. M.: An X-Ray Demonstration of the Nasolacrimal Passageways: Normal and Obstructed, J. Radiol. **3**:521, 1922.

22. Crigler, L. W.: The Treatment of Congenital Dacryocystitis, J. A. M. A. **81**:23 (July 7) 1923.

23. Meller, J.: Occlusion of the Duct in Newborn Children, in Ophthalmic Surgery, ed. 3, Philadelphia, P. Blakiston's Son & Co., 1923, p. 23.

24. Peters, R.: Zur Kenntnis der Atresia ductus-nasolacrimalis congenita, Klin. Monatsbl. f. Augenh. **71**:726, 1923.

25. Rollett: La dacryocystite congénitale et son traitement, Lyon méd. **139**:23, 1927.

26. Lyle, D. J.: Occlusion of the Nasolacrimal Duct in the Newborn, Arch. Pediat. **45**:313, 1928.

27. Campbell, D., and Carter, J.: Stenosis of the Nasolacrimal Passages, Arch. Otolaryng. **9**:367 (April) 1929.

28. Meller, J.: Diseases of the Lacrymal Apparatus, Tr. Ophth. Soc. U. Kingdom **49**:233, 1929.

the duct, but noted that the latter might have to be followed by massage of the sac to bring it back to normal.

Ferrer,[29] in 1930, advocated catheterization of the lacrimal passages in cases of infantile dacryocystitis as promptly as possible after a diagnosis of congenital dacryocystitis is made. He cited at length distressing sequelae of failure to establish patency of the nasolacrimal duct soon after birth. Pesme,[30] in 1931, recommended catheterization of the lacrimal canal as soon as possible after the child was 15 days old and deplored temporizing. Woodruff,[31] in 1931, reported that most of the cases of dacryocystitis of infancy come to the ophthalmologist at about 6½ months of age. A large number require no treatment other than irrigation of the lacrimal sac or, if the duct is not patent, the passing of a probe through it into the nose. Another probe was then passed under the inferior turbinate body, and the two were rubbed together in order to break through and establish a patent lumen.

Jaegers,[32] 1931, described a 1 day old infant with a bilateral swelling of the lacrimal sac. The swelling subsided on the fourth day on one side but required surgical drainage on the other. Majerus,[33] in 1931, observed a case of congenital atresia of the nasolacrimal duct of a colt, similar to that seen in dacryocystitis of the newborn, in which treatment consisted in passing a probe through the lower end of the duct. Charamis,[34] in 1931, described two congenital anomalies of the lacrimal passages: one, a duplicated lower lacrimal punctum that was not permeable; the other, a condition in which the duplicate puncta were both permeable and connected with the lacrimal passages.

Campbell,[35] in 1933, said:

> Tears as a rule are not shed until about three months of age. The accessory glands supply moisture to the conjunctiva and cornea in early infancy.

He suggested treatment of dacryocystitis of the newborn with instillations of silver nitrate and weak epinephrine solution. If this treatment was unsuccessful, he used repeated probings of the duct at four to seven day intervals. Duke-Elder,[36] in 1933, noted "that at the six centimeter

29. Ferrer, H.: Dacriocistitis neonatorum, Vida nueva **25**:207, 1930.

30. Pesme, P.: La dacryocystite congénitale: Aspect clinique; diagnostic; traitement, J. de méd. de Bordeaux **108**:955, 1931.

31. Woodruff, H. W.: Congenital Dacryocystitis, Illinois M. J. **60**:380, 1931.

32. Jaegers, F.: Der Reizkatarrh un die Dakryozystitis der Neugeborenen, Ztschr. f. Geburtsh. u. Gynäk. **100**:42, 1931.

33. Majerus, C. J.: Atresia of the Nasolacrimal Duct (in a Colt), Vet. Med. **26**:225, 1931.

34. Charamis, J. S.: Sur deux cas d'anomalies congénitales des voies lacrymales, Arch. d'opht. **48**:216, 1931.

35. Campbell, R. A.: Dacryocystitis in Infants, Minnesota Med. **16**:267, 1933.

36. Duke-Elder, W. S.: Text-Book of Ophthalmology, St. Louis, C. V. Mosby Company, 1933, vol. 1, pp. 235 and 366.

embryo stage, the lumen of the system is normally open except at the lid puncta and the inferior orifice. The former opens just before the lids separate and the latter at the eighth month.

Riser,[37] in 1935, reported 54 instances of dacryostenosis in children from 1 month to 12 years of age, in 7 of which the condition was bilateral. The average age at which the symptoms appeared was 1½ months. The age at which these patients were first seen by the ophthalmologist was about 6 months. Conservative therapy for two and one-half months resulted in subsidence of the symptoms in 21 cases. In 9 cases probing relieved the symptoms in about three weeks. In 50 per cent, however, relief was obtained with conservative treatment.

In 1935, Schwarz,[38] after examining 207 nasolacrimal ducts in fetuses ranging in age from 3 months to full term, observed atresia of the nasal ostium of the duct in one third of the specimens examined. During the last three months of fetal life the incidence of closed ostiums was practically the same, 35 per cent. The lacrimal sacs and ducts were distended, and large terminal cysts, or bullae, protruded into the inferior meatus if atresia of the nasal end of the duct existed. Fleischer (Erlangen), in commenting on Schwarz's paper, said that the majority of these closed ostiums must open up spontaneously at or soon after birth because congenital atresia of the nasolacrimal duct is rarely observed. Schwarz, in closing the discussion, said that even slight trauma, especially that incident to delivery, is capable of bursting the terminal delicate bulla in congenital atresia. This accounts for the relative infrequency of atresia in early infancy as compared with its great frequency, 35 per cent, in the antenatal material.

In 1935, Bujadoux [39] described a rare congenital malformation of the nasolacrimal duct which he visualized roentgenographically after filling it with a solution of eugenol and a zinc compound. Wokurek and Kraupa,[40] in 1936, stressed the hereditary and familial charcter of congenital occlusion of the nasolacrimal duct on the basis of cases that occurred in their experience. Berens,[41] in 1936, described the lacrimal sac and duct as forming one continuous membranous tube, the sac being

37. Riser, R. O.: Dacryostenosis in Children, Am. J. Ophth. **18**:1116, 1935.

38. Schwarz, M.: Der angeborene Verschluss des Tränennasenkanals, Ber. ü. d. Versamml. d. deutsch. ophth. Gesellsch. **50**:30, 1934; translated, Arch. Ophth. **13**:301 (Feb.) 1935.

39. Bujadoux: Malformation congénitale du canal lacrymal: Emploi en ophtalmologie du plombage eugénol-zinc, Bull. Soc. d'opht. de Paris, 1935, p. 439; Lyon méd. **156**:238, 1935.

40. Wokurek, W., and Kraupa, E.: Der angeborene Tränennasengangverschluss Ztschr. f. Augenh. **90**:273, 1936.

41. Berens, C.: Congenital Atresia of the Lacrimal Duct, in Diseases of the Eye, Philadephia, W. B. Saunders Company, 1936, pp. 27, 39 and 345.

flattened from side to side by the fascia or periosteum sweeping from one crest of the lacrimal fossa to the other. He advocated probing without the use of anesthesia but stated the procedure might have to be repeated several times.

Debroeu and Hermans,[42] in 1937, described an instance of duplicated lacrimal punctum in the lower lid of a 12 year old boy—a congenital anomaly of the lacrimal passages. Chaves Velando,[43] in 1937, cited the relative frequency of dacryocystitis of the newborn simulating purulent conjunctivitis. Gifford,[44] in 1937, said that congenital stenosis is much commoner than is generally believed. He advocated probing through the upper punctum and canaliculus (never the lower) and using a large probe, no. 10 Bowman, even in small infants.

Hardesty,[45] in 1938, reported the incidence of this condition in 1,538 newborn infants as 1.75 per cent. He had observed excessive lacrimation during the first two weeks of the baby's life in some instances. In 34 per cent drainage into the nose occurred during lavage, while in the remainder probing was required to establish drainage. He expressed the belief that it was necessary to clear up the infection in the sac before probing the duct.

Schaeffer,[46] in 1937, again pointed out that the nasolacrimal membrane often remains unruptured at birth. The nasal ostium of the duct may (1) fail of canalization, and its membrane remain intact, (2) be of microscopic size and inadequate for normal function, (3) be buried in mucosa of the lateral wall of the inferior meatus and guarded by a valve-like structure of mucous membrane, or (4) be wide open and adequate. Zentmayer,[47] in 1937, said that in only 1 case in his experience was more than one probing required, and he strongly urged early probing to clear up dacryocystitis of infancy. Harman,[48] in 1938, advocated that the punctum be dilated sufficiently to admit the nozzle of a lacrimal syringe for irrigation.

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42. Debroeu, G., and Hermans, R.: Blépharite par anomalie congénitale des voies lacrymales, Bull. Soc. belge d'opht., 1937, no. 75, p. 109.

43. Chaves Velando, L. A.: Falsas conjunctivitis purulentas del lactante de origen lacrimal, Crón. méd., Lima **54**:373, 1937.

44. Gifford, S. P.: Ocular Terapeutics, Philadelphia, Lea & Febiger, 1937, p. 278.

45. Hardesty, J. F.: Obstruction of the Lacrimal Passages in the Newborn, Am. J. Ophth. **21**:551, 1938.

46. Schaeffer, J. P.: Developmental and Anatomical Factors in Dacryocystitis, Am. J. Ophth. **20**:1252, 1937.

47. Zentmayer, W.: Congenital Imperforations of the Nasolacrimal Duct, Am. J. Ophth. **20**:1256, 1937.

48. Harman, N. B.: Treatment of Minor Conditions in Eye, Brit. M. J. **1**:861, 1938.

Becker,[49] in 1938, described a swelling of the lacrimal sac occurring in two different infants on the second and third days after birth. This was associated with atresia of the nasolacrimal duct at its nasal opening. Even in these newborn infants the sac was observed to be filled with a clear, ropy fluid. The swelling of the sac subsided promptly after probing the duct. Larsson,[50] in 1938, stated that early probing after the discovery of the atresia was an excellent method of treatment and that a single probing usually sufficed. He reported 2 instances of dacryocystitis in which the patency of the duct could not be established by probing and required an intranasal resection of the end of the inferior turbinate body to expose the probe and the duct.

Granström,[51] in 1938, reviewed 640 cases of infection of the sac, 32 of which were of children under 15 years of age. In 13 of these cases the infection was probably due to congenital stenosis of the nasolacrimal duct. The same author,[52] in 1939, reported 28 cases of dacryocystitis in children from 1 to 15 years of age, in most of whom the condition was attributed to neglected congenital stenosis of the duct. Among the patients was a child with loss of vision from a corneal ulcer due to dacryocystitis of the newborn.

Botteri,[53] in 1939, urged pediatricians to differentiate dacryocystitis of infancy from conjunctivitis. He reported on 25 patients, ranging in age from 3 days to 3 months, whom he had treated by pressure over the sac in an attempt to rupture the membrane occluding the lower end of the duct. Wiener and Alvis,[54] in 1939, advocated dilation of the duct with a probe well lubricated with petrolatum U.S.P. MacGillivray,[55] in 1939, reported use of surgical diathermy in destruction of the sac and duct in

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49. Becker, F.: Zum membranösen Verschluss des oberen und unteren Endes des Tränennasenganges, Klin. Monatsbl. f. Augenh. **101**:569, 1938.

50. Larsson, S.: Treatment of Congenital Atresia of Nasolacrimal Duct, Acta ophth. **16**:271, 1938.

51. Granström, K. O.: Die Dakryozystitis bei Kindern, mit besonderer Berücksichtigung vernachlässigter Fälle von kongenitaler Stenoses des Ductus nasolacrimalis, Acta ophth. **16**:512, 1938.

52. Granström, K. O.: La dacryocystite chez les enfants, en considérant spécialment des cas négligés de sténose congénitale du conuit naso-lacrymal, Ann. d'ocul. **176**:836, 1939.

53. Botteri, A.: Ueber die eitrige Entzündung des Tränensackes bei Neugeborenen, Ann. pædiat. **154**:236, 1939; Purulent Dacryocystitis in Newborn, Liljecn. vjes. **61**:277, 1939.

54. Wiener, M., and Alvis, B. Y.: Epiphora of Newborn, in Surgery of the Eye, Philadelphia, W. B. Saunders Company, 1939, p. 405.

55. MacGillivray, A. M.: Infantile Dacryocystitis Treated by Surgical Diathermy, Brit. J. Ophth. **23**:630,, 1939.

several infants with dacryocystitis of the newborn. Busacca,[56] in 1940, advocated the use of Besredka filtrates for irrigating the nasolacrimal duct and sac. About 2 cc. of bouillon containing the Besredka filtrate was used for irrigation every other day until the purulent secretion diminshed.

Velez,[57] in 1941, expressed belief that most cases of dacryocystitis occurred in newborn infants with flat noses. Owing to the improper bony development of the nose, catheterization of the lacrimal canal should not be carried out, but, rather, massage, lavage and general tonic treatment should be used until bony development progresses. Traquair,[58] in 1941, said that the congenital form may be present in several children of the same family. Inheritance from parents who have the adult form is interesting, but its significance is not clear. The congenital form can be easily cured by one passage of a probe or by repeated expressions. The upper punctum was used for probing.

Meek[59] in 1941, said that "if one waits long enough in almost every case, the tearing will clear up, but if one has used conservative treatment until the child is seven months old, one should then probe the duct." He suggested that if constant tearing persists in a baby even after probing, the cause may be tuberculosis, and it is best treated with roentgen radiation. Walker,[60] in 1941, advocated slitting the upper canaliculus and passing a probe with the patient under general anesthesia. Fourteen infants with this condtion were reported in which one such probing permanently relieved the epiphora. Hardesty,[61] in 1941, emphasized irrigation of the sac sufficiently with a large-tipped syringe to clear up the infection before probing was done. In some instances it was necessary to slit the canaliculus sufficiently to insert a Ewing syringe of the large dropper type if the pus was thick.

Judge,[62] in 1941, stated that the imperforate ostium was due to a collection of detritus at the lower end of the lacrimal duct, lying either inside or outside the nasal aperture obstructing the lumen. In some cases

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56. Busacca, A.: Simple Method of Treating Dacryocystitis in Newborn, Arch. Ophth. **24**:1256 (Dec.) 1940.

57. Velez, D. M.: Lagrimeo en los ninos de pecho por falta de desarrollo de los huesos propios de la nariz, An. Soc. mex. de oftal. y oto-rino-laring **16**:317, 1941.

58. Traquair, H. M.: Chronic Dacryocystitis, Arch. Ophth. **26**:165 (Sept.) 1941.

59. Meek, R. E.: Applied Anatomy of the Eye, Arch. Ophth. **26**:495 (Sept.) 1941.

60. Walker, J. D.: Nasolacrimal Stenosis, Texas State J. Med. **37**:544, 1941.

61. Hardesty, J. F.: Obstruction of Lacrimal Passages in Newborn Infant, J. Missouri M. A. **38**:40, 1941.

62. Judge, H. V.: Dacryocystitis of Newborn, New York State J. Med. **41**:25, 1941.

the condition would cure itself spontaneously by sneezing or aspiration. He advocated passage of a small nasal applicator tightly wound with cotton along the under surface of the inferior turbinate body to dislodge a mass of mucous and epithelial cells blocking the duct. "Probing could be avoided in fifty per cent of the cases, twenty-five per cent responding to the nasal approach and the other twenty-five per cent to expression."

Moret and associates,[63] in 1942, reported 14 cases of dacryocystitis of infancy in which irrigation of the sac with saline solution under pressure was used, but some of the ducts had to be catheterized. Naugle,[64] in 1943, reported 4 cases of infantile dacryocystitis, in 2 of which cure had been effected by irrigations with solution of sodium sulfathiazole. Goar,[65] in 1943, advised probing the duct if conservative treatment or lavage of the sac was not successful in clearing the dacryocystitis of the newborn.

In 1945, Arruga[66] reported a case of dacryocystitis of the newborn successfully treated by irrigations of solution of penicillin and probing the duct. Simpson,[67] in 1945, said that it is well known that digital expression of the sac and probing when indicated leads to cure and recovery in the vast majority of cases. He suggested that, in addition to obstruction by an epithelial plug, infection may form a mucoid plug, which may be removed by digital pressure or syringing. Oral chemotherapy (sulfadiazine) was used, together with manual expression of the sac, with recovery in 2 cases.

Gifford,[68] in 1946, suggested that the condition could be familial and hereditary and said that probing the lacrimal passages may be used to cure the mucocele in infants, but only as a last resort, and not until the child is 6 to 9 months old. Too early probing or the use of large instruments may lead to permanent strictures and serious later complication.

PRESENT STUDY

One hundred cases of dacryocystitis in infancy which I have treated during the past few years have been reviewed as to age, sex, side affected, symptoms, type and duration of treatment, complications and end results.

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63. Moret, R. L.; Damianovich, J., and Freyre, A. V.: Obstruction, Causing Conjunctivitis of Infants, Semana méd. **1**:419, 1942.

64. Naugle, T. C.: Treatment of Dacryocystitis in Children: Effects of Sulfathiazole, Sulfonamide, Mississippi Doctor **20**:411, 1943.

65. Goar, E. L.: Infantile Dacryostenosis, M. Rec. & Ann. **37**:611, 1943.

66. Arruga, H.: La penicilian en un caso de dacriocistitis congenita grave, Arch. Soc. oftal. hispano-am. **5**:133, 1945.

67. Simpson, G. V.: Sulfadiazine (Sulfonamide) in Treatment of Dacryocystitis of Newborn, Arch. Ophth. **33**:62 (Jan.) 1945.

68. Gifford, H.: Surgery of the Lacrimal Apparatus, American Academy Ophthalmology, Graduate Lecture Brochure, 1946, course no. 229.

This study has led to the conclusion that the cause of dacryocystitis of the newborn is congenital atresia of the lacrimal duct and that this anomaly should be corrected as early as possible. Conservative symptomatic treatment, instead of early probing of the duct, caused distention, prolonged unnecessary inconvenience, damage and at times permanent injury to the lacrimal passages.

The onset of symptoms, watering of or mucous secretion in the eye was noted in most instances (85 per cent of cases) on the day that the child was brought home from the hospital. This was usually the ninth or tenth day post partum. Whether this was actually the date of onset, or whether the condition may have antedated the tenth day, I am trying to determine by means of an examination made by the hospital nurses in charge of the nursery. So far, in spite of examination by pressure over the lacrimal sac with a cotton-tipped applicator, only a rare case of dacryocystitis among the hospital's newborn infants has been found. The first care of the eyes evolves on the mother on the day that she brings the child home from the hospital, and her thorough examination and search for defects may account for the large number of cases noted on this day. The baby's first contact with outside cold air, when taken from the nursery and exposed, may be the inciting factor in the tearing and may account for the onset of the dacryocystitis on the day that the infant is brought from the hospital. In the other 15 per cent in whom symptoms appeared later, from several weeks to eighteen months after birth, various factors may be involved. The average age of appearance of tears is about 1 month; hence, the symptoms do not appear in some babies until nature discovers that the lacrimal duct is not patent. The instances in which the symptoms, watering and pus from the lacrimal sac, have not appeared until later, from two to eighteen months after birth, may be due to an inadequate ostium together with a superimposed infection of the sac, which has increased the obstruction. Schaeffer demonstrated such ostiums, small, shallow and slanting, in nasolacrimal ducts running beneath the nasal mucosa, with folds and valves obstructing them. In such instances the duct may be patent enough until swelling of the nasal mucosa or venous plexus obstructs it during an allergic episode or an attack of coryza.

The 100 babies with dacryocystitis in my series were almost equally divided as to sex. Heredity or a familial influence was not a factor that could be said to have a bearing on the incidence of this malady. Neither the parents nor their near relatives had a history of dacryocystitis. There were no two children of the same or of related families in the series. Heredity and a familial tendency were inquired into in order to substantiate or to disprove one of the etiologic theories suggested by several authors (Traquair,[58] Kraupa,[8] Gifford[68] and Peters[24]).

In this series of cases, the dacryocystitis occurred in 43 on the left side, in 43 on the right side and in 14 bilaterally. In the development of the nasolacrimal duct, there is, of course, symmetric growth of each side of the embryo, and the junction of the lower end of the duct with the nasal mucosa is probably effected simultaneously in the two ducts. The formation of the opening of the ostium into the nose may not occur in a high percentage of newborn infants until rupture of a membrane at the lower end of the duct occurs to establish patency of the duct. It is probable that on one side the membrane would rupture before the other or that the child might be born with both ostiums unruptured.

The average age at which these infants appeared in the opthalmologist's office for treatment was 3 months. The ducts of 9 infants were probed during the first month of life, those of 19 others by the eighth week and those of 5 others by the eleventh week. The ducts of 13 more were probed during the third month, or a total of 46 per cent of the infants were seen by the third month. As pediatricians have realized that dacryocystitis in infancy can be cured so easily, they have not prolonged conservative treatment unnecessarily, but have sent the baby earlier to the ophthalmologist. I still find an occasional child who has had purulent dacryocystitis for seven to twelve months because the parents have been warned against probing the duct until the child is at least 6 months of age or older (case 59).

The symptoms that the child presents are tearing with mucous or purulent secretion in the eye. The conjunctiva is usually not inflamed; neither is there conjunctival or ciliary injection. Pressure over the lacrimal sac may cause an outpouring of mucous or purulent secretion into the inner canthus of the eye. The sac may be palpably or visibly distended. It refills and can be evacuated into the conjunctival sac several times a day. An attempt to wash the sac with a lacrimal syringe and cannula results in regurgitation into the inner canthus of the eye, while none of the solution goes through into the nose. Ordinarily, there is no redness or inflammatory swelling of the sac. Acute inflammation of the sac is usually secondary to chronic inflammation. In acute dacryocystitis, inflammatory symptoms are usually severe, with redness and swelling over the region of the sac, often so severe as to resemble erysipelas of the face. It is interesting that of this series of 100 cases of chronic dacryocystitis treated by probing, which theoretically should have incited an acute dacryocystitis at least in some instances, dacryocystitis occurred in only 2 (cases 1 and 57), and in both the abscess had antedated the probing.

A review of these cases of dacryocystitis of infancy reveals that in most of them there had been previous lavage, massage, attempts at expression by force and instillations of antiseptic drops. Several infants

had had chemotherapy, and some had had penicillin to clear up the dacryocystitis before they were brought to an ophthalmologist. The treatment used for all these babies at their first visit consisted in probing the nasolacrimal duct in order to establish its patency and irrigating the duct into the nose. Anesthesia was not used except in a few instances in which the size of the child or the apprehension of the parents, the referring physician or the infant seemed to make its use imperative. The success of the treatment depended in part on immobilizing the child so securely that the head could not be moved while the duct was being probed.

It is probably superfluous to describe the swathing, but immobility is such an essential part of the treatment that its explanation is too important to be omitted. The child is placed on a sheet, folded to a size of about 3 by 5 feet (9 by 152 cm.). The arms extended at the child's sides are secured by wrapping first one end of the sheet over the front and tucking it under the back; then the other end of the sheet is brought over the front of the already wrapped bundle and under the back. The sheet is drawn securely tight around the extended legs and knees to prevent kicking or use of the legs or feet and to bind the legs together. The nurse now leans over the right side of the infant, holding the shoulders down with her forearms, while the head is held in her two hands to prevent its wiggling. With the illumination above and behind, the operator sits at the head of the child looking down into the lower lacrimal punctum. A 2 cc. syringe containing isotonic solution of sodium chloride and fitted with a no. 23 gage, 1 inch (2.5 cm.) lacrimal cannula is introduced into the lower punctum after slight dilation with a punctum dilator. As soon as the cannula engages the punctum, it is turned horizontally and slipped through the lower canaliculus until it strikes the bony wall of the lacrimal fossa. As the tip is held firmly against the osseous wall, the syringe is turned vertically and the cannula is directed almost vertically downward in the direction of the nasolacrimal groove. The cannula slides easily into the duct and downward until it pierces the lower end of the canal and its tip rests on the floor of the nose. Some of the solution may be ejected from the syringe into the sac to irrigate it as the cannula enters the sac. As soon as the cannula enters the inferior meatus, having penetrated the lower end of the occluded duct, some solution is injected to insure that the duct is now patent. The infant usually swallows or coughs, indicating that the solution is running into the throat and that the duct is unclogged. The cannula, attached to the syringe, is used instead of the solid Bowman probe so that the entire procedure, the irrigation and the probing, can be carried out with one instrumentation of the duct. A larger probe than the no. 23 gage cannula has not usually been found necessary. A solution of penicillin is used for instillation at home until the child is returned for a subsequent visit, five to seven days later. The symptoms, the mucus

in the sac and the watering of the eye, usually disappear within a few days after probing. If at the next visit the sac still contains pus, it is irrigated again by the same method, and if the duct is not yet patent it is again probed to reopen the closed aperture. It is at times found closed, and cannot be irrigated with the solution until the canal is again probed into the nose.

Duration of Treatment

No. of Cases	Length of Treatment	Average Age at First Visit, Mo.
1	6 mo.	11
1	4 mo.	5½
4	4 wk.	4½
12	3 wk.	5.2
5	2 wk.	8
10	1 wk.	6
67	A few days	3

In an analysis of the reason that these obstructions did not always clear up promptly after probing, it is necessary to review some cases separately. In case 21, the baby, 11 months old, had had purulent right dacryocystitis since the age of 2 months. After the duct was probed, the parents, although advised to return with him in one week, did not do so until two and one-half months later; the sac, still distended with mucopurulent secretion, was washed and the patency of the duct re-established. The parents were uncooperative and difficult to manage and brought the child only irregularly for six months.

In case 73, the child, 5½ months old, had had an infection of the tear sac of the right eye since his tenth day of life, with a great deal of thick discharge. Improvement followed the first treatment, but he was not brought back for seven weeks. As so often happens when the infection of the sac smolders along, it becomes much more difficult to cure. Treatment with sulfonamide drugs, together with expression of the sac, irrigation of the eye and instillation of antiseptic drops twice a day, as well as weekly or biweekly irrigations of the sac, was carried out for two months. The duct was patent, but the sac had no tonicity and remained flabby, distended and infected. It finally cleared up four months after the first visit and remained clear.

The older age of some of the children, as well as the failure of the parents to follow through with treatment after the patency of the duct is established, are both factors in their prolonged symptoms. When the sac has been distended for several months with a mucopurulent infection, its walls are weakened, its tonicity is diminished and its recuperative ability is impared. In order to clear up the dacryocystitis, it is necessary not only to probe the duct to insure its patency, but to treat the lacrimal sac, relieve the congestion and be sure that the patent duct functions. The follow-up treatment, that is, on the second visit soon after the duct is probed, is just as necessary as the original probing, to assure the adequacy of the lumen.

In 67 cases the symptoms disappeared promptly after a single probing, and in another 10 cases they lasted only one week. Considering that the dacryocystitis had existed in most instances since the child was 10 days old and the average age at which the infant was brought for treatment was 3 months, the lacrimal sacs had good recuperative ability. Before the ducts were probed, the infants had had symptomatic treatment since their disease had started, but this had been ineffective. The infants who were treated by probing within the first two months of life were almost without exception cured promptly by a single probing. It is possible that the dacryocystitis might have subsided spontaneously, as the advocates of conservative treatment will rightly point out, if time had been given the structures to develop normally. On the other hand, the prolonged irrigation and massage in some of the older groups would indicate that radical, early treatment may be the most conservative type of therapy.

Some of the complications are of interest and value to consider. Acute dacryocystitis, as has previously been mentioned, was observed in 2 infants, but in both before probing was used. After surgical drainage or rupture of the distended sac, the dacryocystitis was later successfully treated by probing. Eczema of the eyelid occurred once. Mild recurrence of the symptoms during acute coryza or allergic rhinitis was occasionally observed, but in these cases the duct was found to be patent to irrigation. In 1 instance (case 49) a false passage was made by the lacrimal cannula, and edema of the tissues of the lower lid occurred when the saline solution was injected. The cannula was withdrawn and reinserted into the upper punctum and canaliculus. One extra washing a week later was required, but there were no untoward symptoms from the false passage, and the dacryocystitis had entirely cleared up within fifteen days. In case 45 the duct was repeatedly blocked on three successive weekly irrigations. The fluid could be forced into the nose only after the cannula would puncture the nasal end of the lacrimal duct into the inferior meatus. This must have been due either to rehealing of the ruptured membrane of the ostium or to a submucous type of duct, with a very small ostium.

In reviewing the subject of dacryocystitis of infancy, the embryonic development of the nasolacrimal duct is the most important factor in the causation of the disease. The development of the duct from the epithelial cordlike thickening of epidermis along the line of the naso-optic groove, its growth into the mesenchymal tissue, its detachment from the surface ectoderm, its canalization, the formation of lid and nasal sprouts of the mother cord, their contact between the eyelids and the nasal mucosa, the formation or lack of formation of the ostiums, all have been described in the literature cited. The nasal ostium of the nasolacrimal duct may not be

patent in a large percentage of newborn infants. There is a membrane over the lower end of this duct which is said to open at birth. The incidence of dacryocystitis of the newborn depends on the patency of this ostium, and in cases in which it is not patent symptoms of tearing and mucus in the infants' eye appear at about the time that the child is brought home from the hospital. Conservative treatment is probably effective in some instances, or at least at times the duct opens spontaneously, without probing. If the symptoms persist until the third month, the child is usually brought to an ophthalmologist for treatment.

The treatment advocated is probing of the nasolacrimal duct to establish the patency of its nasal ostium, followed by irrigation of the sac and duct. Prolonged conservative treatment, which has been advocated by many earlier and some later authors, is a nuisance to both the parents and the child, and is likely to result in prolonged and permanent injury to the lacrimal passages. It is not necessary to use large probes to establish the patency of the duct; one need only to insure a lumen by perforating the membrane at the nasal ostium. In the cases of dacryocystitis in which early probing was used recovery was prompt, and no untoward results of injury were experienced. In the American or the foreign literature I could find expressed only fears as to what might happen with early probing, and no evidence to substantiate the belief that injury resulted from early instrumentation. In my own cases, and in those of the ophthalmic literature, probing the duct (like pushing a stylet through an obstructed hypodermic needle) cleared the dacryocystitis in most instances with a single probing.

Several questions, however, remain to be answered. At what age do tears first start? Why does dacryocystitis of the newborn seem to start on the first day that the child comes home from the hospital? What percentage of newborn infants have an open nasolacrimal duct at birth? What is the incidence of dacryocystitis of infancy? Why does mucus distend the sac within a few days after birth in some cases? When the nasal ostium is not patent, why is the nasolacrimal duct distended in stillborn or in mature fetuses?

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SPECTRAL TRANSMISSION OF THE EYE TO ULTRAVIOLET RADIATIONS

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Quantitative determinations of the absorption of ultraviolet radiations by different structures of the eye are of importance, since various pathologic conditions, such as cataract,[1] retinal damage [2] and functional visual disturbances,[3] have been variously ascribed to these radiations. The measurements of absorption of ultraviolet radiations by ocular media made heretofore have been limited to photographing narrow bands of radiations transmitted through the eye. As pointed out by the author of one of these papers,[4] the data obtained by this means are qualitative, since it is difficult to estimate the proportion of the radiations which is transmitted through the ocular structures. In the present study quantitative information was obtained by measuring photoelectrically the fraction of radiation which was transmitted.

MATERIALS AND METHODS

All the measurements were made on the eyes of young adult albino rabbits, weighing approximately 2 Kg. Technics used in determining the absorption of ultraviolet radiations for the different portions of the eye follow:

Corneal Epithelium.—The epithelium was removed as a continuous sheet by gently teasing it loose from the stroma with a scalpel while simultaneously directing a fine stream of water under the surface of the loosened edge. Extreme care had to be taken to avoid tearing the epithelium, and many failures were encountered before an

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From the Howe Laboratory of Ophthalmology, Harvard Medical School, and the Massachusetts Eye and Ear Infirmary.

1. Burge, W. E.: The Production of Cataract, Arch. Ophth. **47**:12 (Jan.) 1918.

2. Birch-Hirschfeld, A.: Die Wirkung der ultra-violetten Strahlen auf das Auge, Arch. f. Ophth. **58**:469, 1904. Duke-Elder, W. S.: A Histological Study on the Action of Short-Waved Light upon the Eye, with a Note on "Inclusion Bodies," Brit. J. Ophth. **13**:1, 1929.

3. Wolf, E.: Effects of Exposure to Ultra-Violet Light on Subsequent Dark Adaptation, Proc. Nat. Acad. Sc. **31**:349, 1945.

4. Graham, W. P.: The Absorption of the Eye for Ultraviolet Radiations, Am. J. Physiol. Optics **4**:152, 1923.

intact sheet of epithelium was obtained. To avoid tearing consequent on the use of forceps, the separated epithelium was floated in water and, while still immersed, was placed between two thin quartz cover slips.

The epithelium was relatively clear, although some swelling may have occurred as a result of the use of water in removing the tissue.

Whole Cornea.—The cornea was removed from the eye and placed between two polished plates of quartz, the surfaces of which were ground to match the curvature of its inner and outer surfaces.[5]

Aqueous and Vitreous Humors.—These fluids were taken from a rabbit freshly killed and were placed in quartz microcells of a size to give an optical path of 1 cm. The absorption data for the aqueous humor were recalculated to correspond to the thickness found in the rabbit eye, i.e., 3.2 mm. Since the thickness of the vitreous humor in the rabbit is approximately 1 cm., the data obtained with this medium did not have to be recalculated. With both media the results were adjusted to take into account the loss of about 10 per cent due to the reflecting surfaces of the container.

Lens.—The lens, with the capsule intact, was carefully removed and placed in a specially constructed lucite chamber to hold it immobile. Quartz cover slips were held lightly against the anterior and posterior surfaces of the lens to prevent a focusing action. The lenses weighed approximately 300 mg. each.

Whole Eye.—A chamber of design similar to that used for the lens measurements was made to hold the whole eye. A hole approximately 3 mm. in diameter was cut through the coverings in the back of the eye, and a plain surface quartz cover slip was held against the posterior portion of the eye to prevent loss of vitreous. The radiations traversed the eye in a posteroanterior direction. No quartz cover slip was used on the anterior surface of the eye.

The measurements of absorption of ultraviolet radiations were made with a Beckman spectrophotometer. In order that the beam of radiations should be smaller than the opening cut through the back of the eye, and also smaller than the pupil, a penny in which a 1.3 mm. hole had been drilled was inserted just beyond the exit slit of the instrument. This modification was also employed in using the microcells for determining the absorption of the aqueous and vitreous humors.

The exit slit of the spectrometer was set at 2 mm. The width of the wave band at 400 millimicrons was approximately 10 millimicrons, and that at 250 millimicrons, 2.3 millimicrons.

To prevent leakage of vitreous humor in making the absorption measurements for the whole eye, the spectrophotometer was turned on end. In all instances the sample to be measured was fastened to the sliding mechanism used ordinarily to contain the absorption cells. The sample could thus be moved into and out of the path of radiations in the usual manner.

RESULTS

The per cent of absorption of various wavelengths of radiant energy by the corneal epithelium, cornea, ocular media and the whole eye is shown in figure 1. The curves show that all but approximately 1 per cent of the ultraviolet radiations of wavelengths shorter than 350 millimicrons

5. The quartz plates were obtained from A. D. Jones Optical Works, Cambridge, Mass.

are absorbed by the whole rabbit eye and that the lens is chiefly responsible for this absorption. The cornea and aqueous and vitreous humors absorb most of the radiations of wavelengths shorter than 300 millimicrons,

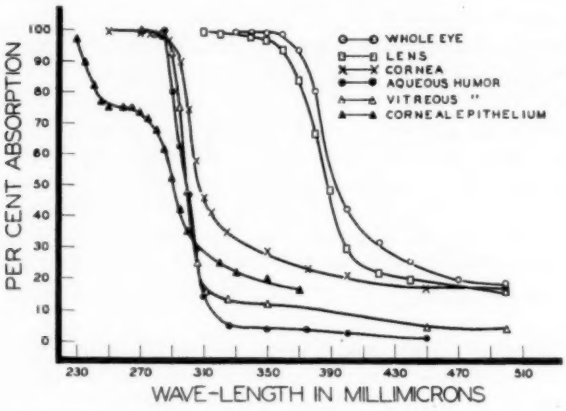

Fig. 1.—Percentage of absorption of ultraviolet radiations by various constituents of the eye.

i.e., the abiotic portion of the ultraviolet spectrum. The corneal epithelium absorbs chiefly radiations of wavelengths shorter than 290 millimicrons.

In figure 2 the proportion of the total radiant energy incident on the outside of the eye which reaches the anterior surface of the various ocular

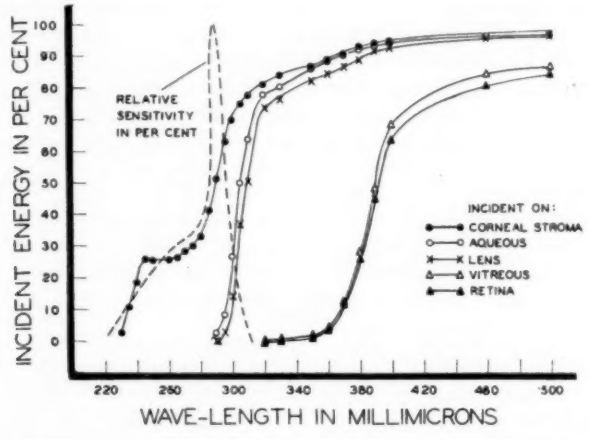

Fig. 2.—Percentage of ultraviolet energy incident on the outside of the eye which reaches the anterior surface of the various ocular media, plotted as a function of the wavelength.

media is shown plotted as a function of wavelength. (The exact values are given in table 1.) For purposes of comparison, a curve (broken line) showing the relative sensitivity of the cornea to radiant energy of various

wavelengths is also shown in figure 2. The series of curves shows the progressive decrease with shorter wavelengths in the amount of radiant energy reaching the various interior portions of the eye. It will be seen, for example, that the ocular tissues in front of the retina absorb essentially all of the radiations producing abiotic effects, i.e., those of wavelengths shorter than 310 millimicrons, and that only a small proportion of the radiations in this region reach the anterior surface of the lens.

COMMENT

The correspondence of the absorption peak, observed for corneal epithelium (265 millimicrons, fig. 1) with that for nucleoprotein suggests that this substance is chiefly responsible for the absorption of ultraviolet

TABLE 1.—*Percentage of Energy Incident on the Corneal Epithelium Which Impinges on the Anterior Surface of the Various Ocular Media*

Wavelength, Millimicrons	Corneal Stroma	Aqueous Humor	Lens	Vitreous Humor	Retina
230	2.7	.....	.....	.....	.....
235	10.8	.....	.....	.....	.....
240	19.0	.....	.....	.....	.....
245	26	.....	.....	.....	.....
250	26	.....	.....	.....	.....
260	26	.....	.....	.....	.....
265	26.5	.....	.....	.....	.....
270	28.7	.....	.....	.....	.....
275	30.7	.....	.....	.....	.....
280	33.2	.....	.....	.....	.....
285	41.5	.....	.....	.....	.....
290	51.5	2	0.4	.....	.....
295	63.0	8.7	3.2	.....	.....
300	70	27	14.3	.....	.....
305	75	50	37	.....	.....
310	78	64	50.5	.....	.....
320	81	78	74	.33	0.29
330	84	80	76.6	.52	0.45
350	86.5	86	82.5	1.82	1.62
360	88.5	88	84.5	4.2	3.8
370	89.5	90	87	12.1	11.0
380	93*	91.2	88.2	28.2	25.8
390	94*	92.8	91.4	48.5	44.6
400	94.5	94	93	68.5	63.5
450	.....	96	96	84	80.5
500	.....	96	96	86.5	84.0

*By extrapolation.

radiations. Such an interpretation is consistent with the highly cellular nature of the corneal epithelium. The relatively thick absorptive layers of the other ocular components obscure any absorption peaks, so that the nature of the absorbing constituents cannot be inferred from the curves.[6] Presumably, the radiations are absorbed primarily by mucoid and collagen in the cornea, by albumin and globulin in the aqueous and vitreous humors and by the alpha and beta crystalbumin and albuminoid in the lens.

On the assumption that the sensitivity of the lens epithelium to injury at any wavelength is the same as that of the corneal epithelium, the minimal amount of radiant energy to which the eye would have to be exposed

6. Cogan, D. G., and Kinsey, V. E.: Action Spectrum of Keratitis Produced by Ultraviolet Radiation, Arch. Ophth. **35**:670 (June) 1946. Moon, P.: Scientific Basis of Illuminating Engineering, New York, McGraw-Hill Book Company, Inc., 1936, p. 30.

before minimal damage would occur to the lens can be estimated from the data in figure 2, provided the spectral distribution of the radiant energy is known. The method of making such an estimation is as follows. The effectivity of radiations at wavelengths λ for producing injury to the cornea may be represented by the equation $Eff\lambda_c = E\lambda\ S\lambda$ where $E\lambda$ is the energy incident on the outside of the eye and $S\lambda$ the sensitivity of the structure. The total effectivity for a broad band of wavelengths is equal to the sum of the effectivities for each wavelength. The effectivity for producing injury to the lens is given by $Eff\lambda_l = E\lambda I\lambda S\lambda$, where $I\lambda$ is the percentage of the total energy incident on the anterior surface of the lens. In like manner, the total effectivity for a broad band of wavelengths for the lens is the sum of the effectivities for each wavelength. The dose to which the eye would have to be exposed to produce minimal damage to the lens is the amount necessary to injure the cornea multiplied by the ratio of the total effectivities.

The procedure may be illustrated in the case of an eye exposed to sunlight. The distribution of the radiant energy in the ultraviolet end of the spectrum is shown in column 2 of table 2. The other values in the

TABLE 2.—*Relative Effectivity of Radiant Energy on the Cornea As Compared with the Lens Epithelium*

λ	$E\lambda$	$I\lambda$	$S\lambda$	$E\lambda I\lambda S\lambda$	$E\lambda S\lambda$
Wavelength, Millimicrons	Energy Units	Percentage	Percentage		
290	0	0	97	0	0
292.5	1	1	81	0.81	81
295	3.3	3.2	57	6.0	188
297.5	7.5	6.5	44	21.4	330
300	14.8	14.5	32	68.6	472
302.5	45	30	23	310	1,030
305	98.7	44	11	477	1,086
307.5	325	50	3	487	975
310	550	57	0	0	0
			Total effectivity*	1,369	4,162
			Ratio $\frac{4,162}{1,369} = 3.02$		

*Total effectivity expressed in arbitrary units.

table are estimated from figure 2. The total effectivity for the cornea expressed in arbitrary units will be seen to be 4,162, while that for the lens is 1,369 and the ratio of the two is 3.02. It may be concluded, therefore, that the eye would have to be exposed to three times the dose necessary to produce minimal damage to the cornea before minimal injury to the lens could be encountered.

Still higher ratios would be encountered with other sources of ultraviolet radiation in which parallelism between the amount of energy coming from the source and the proportion of energy incident on the lens is not as great as it is in the case of the sun. It is evident, for example, that if a source of ultraviolet light emitted radiations shorter than 290 millimicrons

the ratio between the amount of energy needed to produce damage to the cornea and that required for the lens would tend to become infinite, since essentially no ultraviolet radiation would reach the lens.

Incidentally, the studies of Verhoeff and Bell,[7] in which they exposed eyes to ultraviolet radiation from an arc lamp, experimentally confirmed the conclusions arrived at here, namely, that damage to the lens could result only after severe injury had been produced to the cornea.

It is evident from the absorption curves that so little ultraviolet radiation in the abiotic range reaches the retina that damage from these rays would be extremely unlikely unless the sensitivity of the retina to ultraviolet radiation is much greater than that of other tissues. Experimental evidence in support of this conclusion also comes from the investigations of Verhoeff and Bell, who were unable to detect injury to the retina in monkeys and man after exposure to various doses of ultraviolet radiation.

SUMMARY AND CONCLUSIONS

The ultraviolet absorption spectrums of various components of the rabbit eye have been measured. The limit of transmission for the whole eye is approximately 330 millimicrons; that for the lens, 310 millimicrons, and that for the aqueous and vitreous humors and cornea, separately, approximately 280 millimicrons.

Measurements of the absorption of ultraviolet radiations by the corneal epithelium indicate that the chief absorbing element is nucleoprotein, its limit of transmission being less than 230 millimicrons.

The minimal amount of radiant energy from the sun to which the eye would have to be exposed before minimal damage would occur to the lens was calculated to be about three times the dose necessary to produce minimal damage to the cornea.

The results suggest that so little ultraviolet radiation in the abiotic region reaches the retina that damage from these rays would be extremely unlikely.

243 Charles Street.

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7. Verhoeff, F. H., and Bell, L.: The Pathological Effects of Radiant Energy on the Eye, Proc. Am. Acad. Arts & Sc. **51**:629, 1916.

Miss Jane Whitney gave technical assistance.

REAL SIGNIFICANCE OF CENTERING A CONTACT LENS

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The prevailing method among physicians when centering a contact lens has been to center the cornea of the lens with the cornea of the eye. The cosmetic appearance of the lens is best when the cornea of the lens is thus centered with, and in a way superimposed on, the cornea of the eye. But the optical effect of such centering may or may not be the best. Pronounced displacement of the lens cornea with reference to the cornea of the eye will practically always impair vision. But a slight displacement may definitely improve vision, sometimes considerably so, after the lens has been worn for some time.

To understand what happens, one must consider the optical system of the eye alone and that when a contact lens is worn. The two components of the optical system of the eye are the cornea and the crystalline lens. The latter, as has been shown by Gullstrand, may best be considered as consisting of three lenses, i.e., two concave meniscus lenses enclosing a double convex nuclear lens.

Now, one of the most important requirements for perfect imagery in an optical system is that the component elements be properly centered on a common axis. In the eye such centering is always more or less approximate. What has been termed the optic axis is the imaginary line on which the optical elements are more or less centered. The extent of this centering certainly varies in different eyes and would explain, in part, differences in visual acuity. A spectacle lens adds another element to the optical system of the eye, but it does not materially change the intrinsic centering, good or bad, of the optical system.

When a contact lens is placed on the eye, the cornea of the lens replaces the cornea of the eye in a very real sense. Like the cornea of the eye, it is a thin meniscus lens of high power, separating air from a solution which is practically like the aqueous. The cornea of the eye, situated between the buffer solution and the aqueous, not only loses all its positive refractive power but generally acquires a low minus effect. Its power in situ is approximately —0.50 to —0.75 D. The optical system of the eye is now made up of the lens, cornea and the crystalline lens. The cornea of the eye is merely a low power minus lens placed inside the system between

its two components. The effect of this low power ocular cornea (of less than 1.00 D.) is practically negligible with reference to the centering of the optical system, which has a total power of between 50 and 60 D.

It may be apropos to emphasize here that the power of a contact lens in air has little relation to its power when placed on the eye. In the latter position it is always a very strong convex meniscus lens, comparable to the power of the cornea. Even though it is a plano or a minus lens in the air, it becomes a powerful convex lens when placed on the eye, roughly between +35.00 and +45.00 D.

To get the best optical effect of the contact lens, the lens cornea should be centered with the crystalline lens, which is the other major component of the optical system. Objectively this is impossible, but subjectively it can be done. Objectively, one can center the cornea of the lens with the cornea of the eye. But the centering of the lens cornea with the crystalline lens will depend on how well centered the cornea of the eye is with reference to the crystalline lens. Subjectively, a better centering of the whole optical system may sometimes be obtained by watching the direction of the so-called lag.

Every contact lens lags a little behind the movement of the eye. This may be due to action of the lid or to inertia or to both. A patient wearing a contact lens which seems properly centered in the primary position with reference to the cornea of the eye may see better when he turns his head, say, to the right. What has happened? As his head turned to the right, the eye, say it is the right eye, has turned to the left, that is, nasally. The lens, lagging slightly behind the movement of the eye, is now displaced slightly toward the temple. If this produces better vision, the lens in this position must be more accurately centered with the crystalline lens in the eye than it was before. This maneuver would constitute the subjective centering of a contact lens, which is centering it with reference to the crystalline lens, as against objective centering, which is centering it with reference to the cornea of the eye.

It may be added that the visual axis, the line along which vision actually takes place, is generally oblique to the optic axis by the so-called angle alpha.

This obliquity increases the general aberrational defects of the retinal image and must cause some lowering of visual acuity. But the visual axis is a secondary axis of the optical system of the eye, and it may be postulated that when the optical components are more perfectly centered on the principal, or optic, axis, the image along a secondary axis will be better focused. Of course, it is possible that, taking into consideration the complex structure of the crystalline lens, as well as other aberrational factors, a less perfect centering on the optic (principal) axis may give a better retinal image along the visual (secondary) axis. In either case,

however, the effect is ascertainable only by a subjective centering of the contact lens.

The fact that a contact lens may introduce a new centering and a new optic axis will explain some commonly observed facts. Many patients see somewhat "differently" with a contact lens; there is a different "feel" to the seeing process. Vision frequently improves after a contact lens has been worn for some time over what it was when the lens was first put on. One must visualize in these cases a sort of transformation of one type of eye, with all its aberrational effects, which the patient has learned to interpret, into another type of eye, with different aberrational effects.

One sometimes sees cases of mild conical cornea in which vision is greatly improved by a contact lens. The ophthalmometer will show a highly curved corneal surface but little, if any, irregularity. The striking improvement in vision produced by a contact lens in these cases is probably due to a better centering of the cornea of the lens with the crystalline lens than was obtained with the cornea of the eye. Many other phenomena in work with contact lenses will become clearer if the physician realizes that the contact lens reduces the cornea of the eye to an insignificant position, and itself becomes the most important element in the new optical system of the eye. This is entirely different from the accessory effect on the optical system of the eye produced by a spectacle lens.

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SYNDROME OF UNILATERAL RECURRENT ATTACKS OF GLAUCOMA WITH CYCLITIC SYMPTOMS

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In order to form a complete picture of a case of glaucoma, it is essential to observe the patient at frequent intervals and over a relatively long period. A case, ideal in this sense, presented itself in a physician who lived in the immediate vicinity and thus was able to visit our office at the earliest indication of an oncoming attack. This patient had recurrent unilateral attacks of ocular hypertension associated with cells in the aqueous and a few keratic precipitates, which disappeared shortly after the tension returned to normal. The time relation of the appearance of the hypertension and the cyclitic phenomena could be accurately studied. Also, an attempt was made to evaluate the response of the symptoms to various drugs.

This case aroused our interest in the relation between glaucoma and cyclitis. A survey of our glaucoma files disclosed 7 more such cases, and a new case occurred in our practice during the preparation of this paper. All these 9 cases, which were followed for periods varying from one month to nineteen years, were characterized by a striking uniformity in symptoms, course of the disease and response to treatment.

The chief features of this syndrome may be briefly described as follows:

1. The disease is unilateral. In 3 cases there was some degree of heterochromia, and in each instance the lighter-colored eye was involved. In 3 cases anisocoria was present, the affected eye having the wider pupil.

2. The presenting symptom is usually slight discomfort, colored halos or blurring of vision. However, no symptoms may be present. There is no pain. Vision is usually good, even at the height of the attack.

Read at a meeting of the New York Society for Clinical Ophthalmology, May 5, 1947.

3. The eye is white, or a few dilated conjunctival vessels may be visible. Ciliary injection is never present. If the tension is very high, mild congestion of the sclera or edema of the corneal epithelium may be noted.

4. Ocular hypertension may appear a day or so before, or simultaneously with, cells in the aqueous. It is followed within the next twenty-four hours by from one to twenty small, well defined, unpigmented precipitates on the posterior surface of the cornea. These soon begin to disappear, and, if the hypertension persists, fresh ones may appear. After subsidence of the hypertension, the precipitates fade away within a few days to a month. Although precipitates are present as a rule, they may be absent during some of the attacks (case 3). At no time is there more than a trace of aqueous flare. Posterior synechias are never formed.

5. The angles were open in all 4 cases in which gonioscopic studies were made. In 2 cases they were wide and in 2 moderately narrow.

6. The individual attacks of ocular hypertension have lasted from a few hours to one month, but rarely over two weeks. Attacks which have been observed without treatment have cleared within two weeks. It is possible that overtreatment, whether with miotics or with mydriatics, may prolong the attack.

7. Episodes may occur with varying frequency and without any apparent cause. One patient has had five attacks in a period of eight months; another has been having two or three attacks a year for the past thirteen years, and still another had four attacks up to thirteen years ago and has been free from symptoms since. The visual fields may show enlargement of the angioscotomas during the acute phase. In 1 case, in which there were deep cupping and pallor of the nerve head, the field became progressively contracted. In all other cases the field remained normal during the course of the disease. During the intervals of freedom from glaucoma, provocative tests, such as the liability and the water-drinking test, give negative results, and there are no signs or symptoms either of iridocyclitis or of glaucoma.

8. Treatment does not seem to shorten the course of the attack. One-half to 2 per cent pilocarpine hydrochloride N. F. may lower the tension temporarily. Physostigmine and stronger concentrations of pilocarpine usually give rise to extreme discomfort and pain and may even cause a rise in tension. Homatropine and atropine usually have no pronounced effect on the tension, but, apparently, they are not detrimental to the eye. Epinephrine bitartrate, 2 per cent, and phenylephrine ("neo-synephrine") hydrochloride, 10 per cent, may produce an evanescent reduction of the tension. Since the attack is self limited, it

is safe to procrastinate and use no treatment (or placebo therapy) until the diagnosis has been established and the course has been followed through at least one attack. Surgical intervention did not have to be resorted to in any of our cases. Kraupa[1] found that in 2 of his 4 cases surgical treatment did not affect the subsequent course of the disease, since the patients continued to have acute attacks.

REPORT OF CASES

CASE 1.—E. W., a white physician aged 43, consulted an ophthalmologist because, for the first time, he had experienced blurring of vision for three hours. The tension in the right eye was 70 mm. (McLean), while that in the left eye was normal. A diagnosis of primary glaucoma was made. With use of pilocarpine, the tension dropped to normal but soon rose to 50 mm. (McLean). After several days of therapy with miotics, keratic precipitates were observed in the right eye, and the diagnosis was changed to that of secondary glaucoma. Use of pilocarpine was stopped after one week of treatment. Three days after the discontinuation of the miotic (or ten days after the onset), the tension was 25 mm. (McLean). The patient was free from symptoms except that the left pupil was dilated and accommodation was temporarily suspended, owing to the inadvertent use of atropine sulfate. During this attack his temperature, which was normally below 98 F., rose to 99 F. on three occasions. The white blood cell count rose from 7,000 to 11,100 per cubic millimeter.

When the patient was first seen by us, on Aug. 19, 1946, two weeks after the onset, the tension was 18 mm. (Schiotz) in the right eye and 22 mm. in the left eye. The right pupil was 3.5 mm. and the left 5 mm. in diameter (atropine mydriasis). Both irises were brown, but the right was of slightly lighter color than the left. In the right eye, a few nonpigmented, small, well defined keratic precipitates were present on the posterior surface of the cornea. There were no cells in the aqueous and no posterior synechias. The media were clear, and the fundus was normal. The left eye was normal. Vision was 20/15 in each eye with a —1.75 D. sphere for the right eye and a —2.25 D. sphere for the left eye. Gonioscopic examination of both eyes showed wide angles throughout. The lower part of Schlemm's canal contained blood.

The patch test gave a 3 plus reaction to tuberculin. A roentgenogram of the chest showed no evidence of tuberculosis. Brucellosis was excluded by serologic study. The Wassermann reaction of the blood was negative.

The patient gave a history of old nongonococcic prostatitis and of mild and variable hypertensive vascular disease, as well as of hay fever, of fifteen years' duration, associated with asthma during the first two years.

He remained free from symptoms until October 7, when he presented himself two hours after he had begun to see rainbows with his right eye. At this time tension was 49 mm. in the right eye and 20 mm. in the left eye. The eye was white. There were a few deposits on the posterior surface of the cornea and numerous cells in the aqueous, but no flare was noted. With 1 drop of 10 per cent phenylephrine hydrochloride N.N.R., the right pupil was almost maximal. The tension fell to 41 mm. in forty-five minutes and then dropped to 22 mm. within four hours. The following morning, tension in the right eye was 24 mm., the cells were less numerous but the deposits had increased in number.

1. Kraupa, E.: Ocular Hypertension in Acute Angioneurosis of the Ciliary Body ("Glaucoma Allergicum"): Its Relationship to Cyclitic and Heterochromic Glaucoma, Arch. f. Augenh. **109**:416, 1935.

Another ophthalmologist saw the patient that evening and, finding the tension normal, instilled a drop of homatropine hydrobromide into the right eye. That night the patient had an uncomfortable sensation in his right eye. The following morning, October 9, the right pupil measured 5 mm. and the tension was 53 mm. (Schiotz), while the left pupil was normal. The eye was white except for a few dilated conjunctival vessels. Cells were seen in the aqueous, and a few fresh deposits were visible on the posterior surface of the cornea. This time 10 per cent phenylephrine hydrochloride failed to lower the tension, but 2 per cent pilocarpine hydrochloride brought it down to 20 mm. within two hours. A 3 D. increase in myopia was noted, which lasted two hours. Pilocarpine hydrochloride, 2 per cent, given every four hours, controlled the tension. No cells were observed after October 10 (three days after onset of the second attack). The keratic precipitates, however, persisted until October 24. Miotics were discontinued on October 16, and the tension remained even lower than that in the left eye.

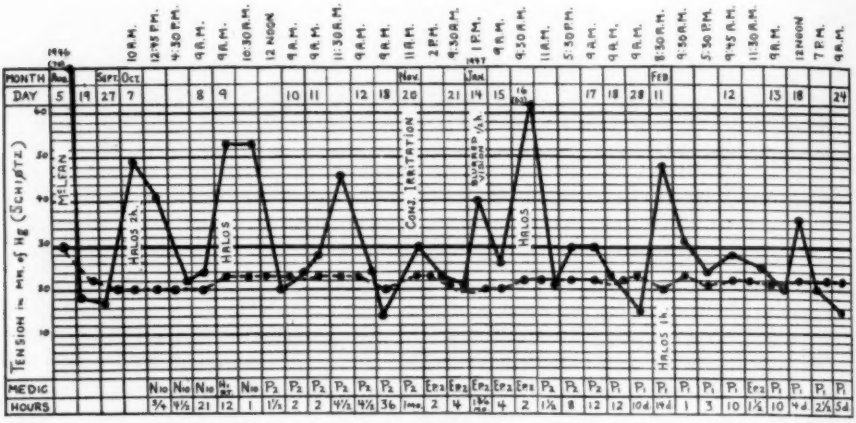

Chart 1 (case 1).—Tension curve for a patient with glaucomatocyclitic crises in the right eye. N_{10} indicates phenylephrine hydrochloride, 10 per cent; H_1 homatropine hydrobromide, 1 per cent; P_2, pilocarpine hydrochloride, 2 per cent; Ep_2 epinephrine bitartrate, 2 per cent; P_1, pilocarpine hydrochloride, 1 per cent.

In this chart, and in charts 2 to 5, the curve for the right eye is shown by the solid line; that for the left eye, by the broken line.

The third episode occurred on Nov. 20, 1946, when the patient experienced slight conjunctival irritation in his right eye. The right pupil was 1 mm. larger than the left. Tension was 30 mm. in the right eye and 23 mm. in the left eye. There were deposits on the posterior surface of the cornea and numerous cells in the aqueous. The patient suggested the use of 2 per cent epinephrine bitartrate. Within three hours the tension dropped to 23 mm. He had no visual disturbance, and the irritation promptly disappeared. The tension remained normal. On Jan. 8, 1947 only two minute keratic precipitates remained.

On Jan. 14, 1947, one-half hour after the onset of blurring of vision and irritation in the right eye, the tension measured 40 mm. in the right eye and 20 mm. in the left eye. There were no cells in the aqueous, and the eye was white. The two precipitates which had been noted previously were still present. Epinephrine bitartrate, 2 per cent, was used every four hours, and the following morning the tension was 26 mm. in the

right eye and 20 mm. in the left eye, but this time a few cells were present in the aqueous and about a dozen new keratic precipitates were noted. In spite of the continued use of epinephrine bitartrate, the tension rose to 62 mm. on the following day (third day after onset of attack). Pilocarpine hydrochloride, 2 per cent, brought the tension down to 21 mm. within an hour and a half and increased the myopia by 4 D. The tension fluctuated around 30 mm. until January 18 (unaffected by use of pilocarpine, epinephrine or phenylephrine). It then dropped sharply to between 15 and 18 mm. On February 4, only one keratic precipitate was visible.

The fifth attack occurred on February 11. It had a similar course. Again, cells were seen and fresh precipitates noted. They disappeared within ten days.

Pupillographic studies, made on two occasions by Dr. Otto Lowenstein, showed a curve which indicated sympathetic phenomena, such as are noted in cases of hypertensive vascular disease. A diurnal tension curve was normal. The water-drinking test, used as a provocative, gave negative results. The tension curve is shown in figure 1.

CASE 2.—M. S., a dentist aged 41, had the first attack of hazy vision and colored halos in the left eye in September 1934, when he was 28 years of age. An ophthalmologist made a diagnosis of low grade cyclitis with secondary glaucoma and treated him with atropine and salicylates. The attack subsided within a few days.

A similar episode occurred in September 1938. A different ophthalmologist treated him at first with pilocarpine for three weeks, then, when keratic precipitates were noted, atropine was substituted. This attack subsided after six weeks. Third and fourth attacks, each lasting three weeks, occurred in August 1939 and February 1940, respectively. In these attacks treatment was with homatropine.

The patient was first seen in this office on May 11, 1940, on the third day following the onset of hazy vision and colored halos in the left eye. The day prior to his visit, he had used 1 per cent pilocarpine hydrochloride, and the symptoms subsided after one hour. Examination showed vision to be 20/20 in the right eye with a correction of —0.75 cyl., axis 170, and 20/15 in the left eye with a correction of +0.50 sph. —1.00 cyl., axis 180. Both eyes were white. The irises were brown and of the same color. The pupils were regular and reacted to light. The right pupil measured 3.5 mm. and the left 4 mm. The fundi were normal. Examination with the slit lamp revealed twelve minute keratic precipitates in the left eye. Both anterior chambers were of normal depth. Tension was 15 mm. in the right eye and 31 mm. in the left eye. The fields and blindspots were normal.

A patch test gave a negative reaction to tuberculin. Medical examination revealed nongonococcic urethritis. The electrocardiogram and the basal metabolic rate were normal. Roentgenograms of the sinuses, teeth and chest revealed a normal condition. The patient gave a history of hay fever due to ragweed.

He was given a 1 per cent solution of pilocarpine hydrochloride to use three times a day in his left eye. On May 15, 1940 the tension in this eye was 22 mm. The precipitates were gone by June 10 (one month after the onset).

The patient returned a few times for examination. The tension was always normal, and no signs of cyclitis were present. On October 15, he was seen three hours after he began to see rainbows and twelve hours after onset of hazy vision in the left eye. The eye was white, but the tension was 38 mm. Tension in the right eye was 17 mm. Vision was normal in both eyes. Examination with the slit lamp revealed eight fresh, discrete, small keratic precipitates. Two hours after use of 10 per cent pilocarpine hydrochloride, tension in the left eye was 31 mm. He used 2 per cent pilocarpine hydrochloride every two hours, and the following day the tension was normal. By November 10 all signs of

cyclitis had disappeared. He continued to use 1 per cent pilocarpine hydrochloride three times a week for one year.

On Feb. 5, 1942 he had another attack of seeing rainbows and hazy vision in the left eye, with recurrence the following day despite the use of 1 per cent pilocarpine nitrate. He was seen on the third day after onset, when tension was 36 mm. in the left eye. Three precipitates were found. Tension in the left eye was normalized in nine days, and the keratic precipitates were gone in three weeks.

He joined the Army and was well until April 1944, when he had another attack and was treated with epinephrine packs in an Army hospital. The tension returned to normal in three days. After his discharge, he had another mild episode on Oct. 17, 1944 and has been well ever since. On his last visit, in February 1947, the right pupil was slightly smaller than the left, but the eyes were otherwise normal.

Pupillographic studies in April 1947 showed a curve similar to that associated with primary glaucoma.

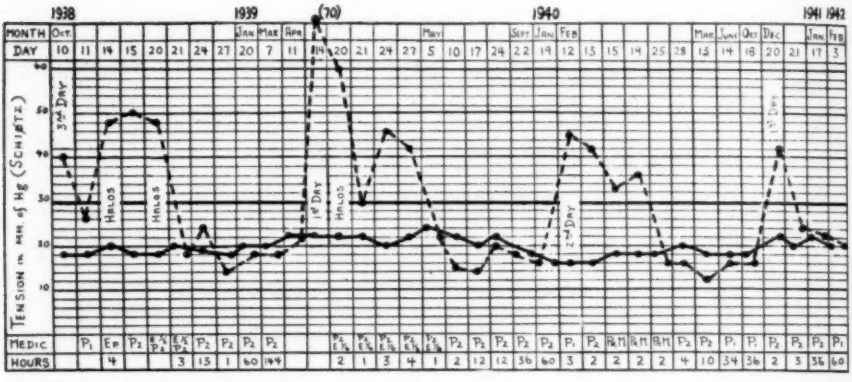

Chart 2 (case 3).—Tension curve for a patient with glaucomatocyclitic crises in the left eye. P_1 indicates pilocarpine hydrochloride, 1 per cent; *E½*, physostigmine salicylate, 0.5 per cent; *Pr.M.*, neostigmine methylsulfate, 5 per cent with methacholine chloride, 20 per cent; *Ep.*, epinephrine bitartrate, 1 per cent; P_2, pilocarpine hydrochloride, 2 per cent; *E* 1/6, physostigmine salicylate, 0.16+ per cent.

CASE 3.—A. S., a physician aged 49, was seen on Oct. 24, 1938, seventeen days after the onset of foggy vision in his left eye. He gave no history of similar episodes. He received treatment from another ophthalmologist, who had found the tension in the left eye to be 40 mm. After use of 1 per cent pilocarpine hydrochloride and 1 per cent epinephrine bitartrate, the tension quickly dropped to 24 mm., but rose again progressively to 48 mm. on October 14 (seventh day of the attack). At this time he saw colored halos around lights. The tension became normal fourteen days after the onset.

Examination revealed vision of 20/20 in each eye with a correction of —5.00 sph. —0.50 cyl., axis 180. The left eye was white. The fundi were normal. Tension was 19 mm. in the right eye and 24 mm. in the left eye (thirteen hours after the last use of a miotic). The fields and blindspots were normal. Examination with the slit lamp showed an atypical Krukenberg spindle in each eye, atrophy of the pupillary border of the left iris and deposits of pigment on the lens capsule. Two white precipitates were present on the posterior surface of the left cornea. These were gone by November 3 (four weeks after onset).

The family history revealed that one other member of the family, an aunt on the paternal side, had glaucoma. The patient had been subject to severe right-sided migraine headaches for the past two years. He has a highstrung, neurotic nature.

On April 14, 1939, he awoke with foggy vision in the left eye, followed by his seeing colored halos. The tension was 22 mm. in the right eye and 70 mm. in the left eye (three days previously the tension had been 22 mm. in each eye). The eye was white. Vision was 20/30 in the left eye. There were cells in the aqueous and a few white precipitates on the posterior surface of the cornea. He used pilocarpine and physostigmine at frequent intervals. Tension fluctuated between 30 and 60 mm. but was normalized by May 5, 1939. The deposits had disappeared by May 24, 1939.

The next episode occurred on Feb. 11, 1940, when the patient began to see rainbows with his left eye. After a few instillations of 1 per cent pilocarpine hydrochloride, the halos disappeared. The next day tension in the left eye was 45 mm. Examination with the slit lamp at this time did not reveal any cells in the aqueous or keratic precipitates. When the hypertension failed to recede after two days, he began to use 20 per cent methacholine chloride with 5 per cent neostigmine methylsulfate. The tension returned to normal on February 25. No precipitates or cells appeared during the entire course of this attack.

On Dec. 20, 1940, the tension rose to 42 mm. and was quickly controlled with pilocarpine. No cells or deposits were noted with this attack. The tension curve is shown in chart 2.

The patient has been free from symptoms and tension has remained normal up to the time of writing. Pupillographic studies showed a bilateral curve similar to that associated with primary glaucoma. He was carefully studied for foci of infection. One abscessed tooth was extracted in May 1939, and he received a course of injections of autogenous vaccine. This treatment failed to influence the course of the attacks. He never saw halos when the tension was below 40 mm., although occasionally he had no visual disturbance with a tension as high as 60 or 70 mm. Miotics increased his myopia by as much as 4 D.

CASE 4.—M. C., a white man aged 45, was first seen on April 21, 1944. He gave a history of having had attacks of blurred vision and seeing colored halos in the right eye every four to six months for the past ten years. These attacks would last three to ten days and wear off without any treatment, leaving no sequelae.

The present attack began on April 18, and had been preceded by a similar episode ten days previously. The patient decided to consult a physician because, for the first time, he had experienced two attacks within so short a period. He had never had any symptoms in the left eye. Examination showed 20/20 vision in the right eye with a correction of +3.50 sph. +0.25 cyl., axis 90, and 20/200 in the left eye with a correction of +3.75 sph. +1.75 cyl., axis 115. The left eye had been amblyopic since childhood. The right pupil was larger than the left and reacted sluggishly to light and in accommodation. Tension was 65 mm. (Schiotz) in the right eye and 28 mm. in the left eye. The fundi were normal. The anterior chambers were of normal depth. Examination with the slit lamp showed a few deposits on the posterior surface of the right cornea. The left cornea was normal. He was given 2 per cent pilocarpine hydrochloride, to be used four times a day. The drops caused pain and blurring of vision, which lasted two hours. The tension continued to be elevated all this time, despite the drops. On May 1 the deposits were much fewer. He was not seen until June 15, when no precipitates were found.

The patient returned again on April 26, 1946, two days after he began to have blurred vision and see rainbows in his right eye. He used pilocarpine of his own accord, but the eye felt worse and he became alarmed. He had had three attacks since he was

last seen (June 15, 1944). The first one, in September 1944, lasted three days and subsided with the use of pilocarpine. The other two, which occurred on Jan. 1 and Nov. 7, 1945, lasted one week each.

There was slight scleral congestion. The cornea was somewhat steamy. The right pupil was larger than the left but reacted normally. The fundus was clearly visible and was normal. The slit lamp showed three deposits on the posterior surface of the right cornea. The tension was 70 mm. in the right eye and 28 mm. in the left eye. Phenylephrine hydrochloride, 10 per cent, and pilocarpine hydrochloride, 5 per cent, failed to affect the tension. In view of this fact, and because of the self-limited nature of the crises, the patient was instructed to use nothing but acetylsalicylic acid and ice applications. On May 3 the symptoms subsided, and the tension remained normal until Dec. 25, 1946. At this time he consulted another ophthalmologist, who found that the tension was 50 mm. in the right eye and that precipitates were present on the posterior surface of the cornea. This attack subsided in ten days.

The patient was last seen on March 9, 1947, when the right eye appeared perfectly normal. The fields and blindspots were normal. Gonioscopic examination showed the angles to be moderately narrow. The right pupil was 0.5 mm. larger than the left. No heterochromia was noted. Pupillographic studies showed central sympathetic phenomena. The patient has no systemic disease and is not subject to any allergic manifestations.

CASE 5.—E. T., a white woman aged 32, came to our office on Oct. 30, 1939. She gave a history of an attack of blurred vision in the right eye on Aug. 15, 1939. Another ophthalmologist had prescribed pilocarpine, and the attack wore off in one day. She continued to use pilocarpine and physostigmine, but she had another attack in the right eye on October 23. The tension did not respond to miotics at this time, and surgical intervention was advised but was not carried out because the eye began to improve soon thereafter.

The patient was slender and somewhat underweight and appeared tense and excitable. She had no family history of glaucoma. No history of allergy was given. Examination showed vision of 20/20 in each eye with a —0.75 D. sphere. The pupils were pinpoint, owing to the use of miotics. Tension was 31 mm. in the right eye and 20 mm. in the left eye. Examination with the slit lamp showed that the anterior chambers were of normal depth. There were about six small, discrete, white deposits on the posterior surface of the right cornea. The fields and blindspots were normal. Thorough medical examination disclosed no pathologic condition. Roentgenograms of the sinuses revealed nothing abnormal, but two impacted teeth were discovered and removed. Use of pilocarpine hydrochloride, 1 per cent, twice a day, was continued. The symptoms did not recur, and the tension remained normal. The keratic precipitates disappeared by November 24 (four weeks after onset).

The patient remained well until Jan. 1, 1940, when she noticed haziness of vision and rainbows in the right eye. This attack coincided with the end of the menstrual period. She was seen on January 3, when the tension was 42 mm. in the right eye and 22 mm. in the left eye. Vision was normal, and the eye was white. There were eight minute deposits on the posterior surface of the right cornea. Tension subsided by January 5 with the use of pilocarpine, and the deposits disappeared by January 23. She has remained well since this time.

CASE 6.—E. D., a white man aged 59, a pharmacist, had been subject to recurrent attacks of slight pain and blurring of vision every few months for ten to fifteen years prior to his first visit to our office, on March 9, 1936. The present attack occurred on March 2 and was the severest he had yet had. When he was first seen by another

ophthalmologist, on the fourth day of his attack, a diagnosis of acute glaucoma was made and operation was advised. A second ophthalmologist, however, treated him with 2 per cent pilocarpine hydrochloride and 0.25 per cent physostigmine salicylate. The attack subsided and vision improved. Thus, the attack lasted one week. The patient had a mild hypertensive vascular disease. There was no family history of glaucoma.

Examination showed vision of 20/20 in the right eye with a correction of +0.25 sph. +0.50 cyl., axis 180 and 20/15 in the left eye with a correction of +1.00 D. sph. +1.00 cyl., axis 75. The right eye was normal in appearance except that the right iris was gray and the left one brown. The right pupil was smaller than the left because of the use of pilocarpine. The right disk was pale and showed moderate glaucomatous excavation. The left eye was normal. Examination with the slit lamp showed two unpigmented deposits on the posterior surface of the right cornea. The tension was 22 mm. in each eye. There was absence of the upper half of the right field, with a pronounced contraction of the lower half. The left field was normal.

During the two years following this attack, the patient used pilocarpine irregularly once or twice a week; the tension remained normal, and no keratic precipitates were seen. On June 7, 1938, the tension was found to be 36 mm. The patient had had symptoms of blurred vision for the past few days and, although the eye (right) was white, examination with the slit lamp showed several fresh, well circumscribed deposits on the posterior surface of the cornea. Tension responded to 1 per cent pilocarpine hydrochloride, and the symptoms subsided.

On June 14, 1940 another routine check-up revealed that tension in the right eye was increased. In July the tension was back to normal; but it rose again on Oct. 25, 1940, and fresh deposits were noted. The hypertensive phases became more frequent after November 1940. Although the patient did not have any symptoms, the visual field in his right eye rapidly diminished, and vision was reduced to light perception by June 1941. He instilled pilocarpine irregularly, and only when he thought he had increased tension. This drug, although it usually lowered the tension, did not prevent attacks.

CASE 7.—R. M., a white housewife aged 51, began to have attacks of edematous swellings in various parts of the right side of the face and neck, associated with headache and misty vision of the right eye, in the summer of 1927. (She was 31 years of age at this time.) An ophthalmologist found the tension in the right eye to be 70 mm. and prescribed pilocarpine. The following day the tension was normal. She continued to use low concentrations of pilocarpine. Her tension remained normal, but in June 1933 she complained of blurred vision in the right eye, of two days' duration. The eye was white. The tension was 43 mm., and a few fresh keratic precipitates were present in the right eye. This time she was given homatropine, and the tension subsided within three days. Medical examination showed no foci of infection. The precipitates disappeared within three weeks. In February 1934 she had a similar episode. Tension was 31 mm., and a few fresh deposits were noted. This attack improved in a few days with the use of homatropine. The drug was continued prophylactically for nine months. During the next year she had another attack and was treated with pilocarpine.

When she came to this office, on May 23, 1942, she had been using miotics in the right eye for the past few years. Tension was 17 mm. in the right eye and 19 mm. in the left eye. Vision was 20/25 in each eye with a correction of —2.50 cyl., axis 45 for the right eye and —1.75 sph. —2.00 cyl., axis 135 for the left eye. The irises were brown and of the same color. The fundi were normal. The media were clear. The anterior chambers were of normal depth, and gonioscopic examination showed that both angles were open and wide. Examination with the slit lamp revealed nothing abnormal.

The patient has been followed at monthly intervals up to the present. At no time during this period, from 1942 to 1947, were any deposits noted on the cornea or were cells present in the aqueous, and the tension remained consistently normal in each eye. The patient has used 0.5 per cent pilocarpine hydrochloride twice a day in the right eye, mainly for psychologic reasons. During this time, her health has been good, but a mild hypertensive vascular disease developed.

Pupillographic examination on March 13, 1947, after the patient had discontinued use of pilocarpine for one week, showed a bilateral curve similar to that found in cases of primary glaucoma. The lability test produced no increase in tension. The fields were normal.

CASE 8.—L. E., a housewife aged 43, first seen on March 12, 1947, one week after the onset of blurred vision and "itching" in her right eye, had had a similar attack one year before but did not consult a physician. This time she visited an ophthalmologist, who found a tension of over 70 mm. in her right eye. The eye was white, and no keratic precipitates were noted at this time. He instilled a drop of 0.5 per cent physostigmine salicylate into her right eye, whereupon the eye became inflamed and tender to touch. The tension remained high. Examination by us the following day revealed that her right eye was white and that tension was 77 mm. in the right eye and 24 mm. in the left eye. The iris of the right eye was a light gray, whereas that of the left eye was brown. Examination with the slit lamp revealed approximately seven translucent, small, round precipitates on the posterior surface of the cornea of the right eye. The left eye was normal. The fundi and fields were normal. Vision was 20/20 in each eye without correction. Gonioscopic examination showed that both angles were moderately narrow, the corneoscleral trabeculum was somewhat pigmented and Schwalbe's line was indistinct. Phenylephrine hydrochloride, 10 per cent, lowered the tension in the right eye to 56 mm. She was instructed to do nothing to the eye except to apply cold compresses. She was comfortable thereafter, and the tension gradually fell, becoming normal by March 19 (fifteen days after onset). On March 26 the keratic precipitates were disappearing. The pupils were equal in size.

Her medical history was interesting. For many years she had been subject to attacks of migraine and crying spells. Her blood-pressure was 160 systolic and 100 diastolic. In 1937 she had a cholecystectomy for typical recurring attacks of cholecystitis. The attacks continued to recur for several years after the operation. Each episode was followed by urticaria on the right side of the face and neck, extending to the right half of the forehead and the back of the right hand. The urticaria was associated with tearing of the right eye. No cause was found for these urticarial attacks. The patient did not have hay fever. Pupillographic examination showed central sympathetic phenomena similar to those found in patients with hypertensive vascular disease.

CASE 9.—B. T., a woman aged 60, a bookkeeper, had been subject to recurring attacks of blurring of vision in the left eye since 1937. These attacks lasted a few days to one week and recurred every eight to twelve months. Several years ago, she was given 2 per cent pilocarpine hydrochloride by an ophthalmologist, but she did not use this drug regularly because it engendered blurring of vision. Her sister has been under our care for chronic simple glaucoma for a number of years.

The patient came to this office on March 10, 1945, two weeks after the intermittent appearance of rainbows and blurring of vision, which began about one hour after arising in the morning and disappeared toward evening.

Examination revealed vision of 20/20 in each eye with a correction of —0.25 D. sphere for the right eye and —0.25 sph. —0.25 cyl., axis 150 for the left eye. The ten-

sion was 25 mm. in the right eye and 84 mm. in the left eye. The ciliary body was not injected, but the sclera showed slight generalized congestion. Ophthalmoscopic examination showed a large, irregular-shaped opacity in the vitreous of the left eye in front of the disk. The nerve head was of normal color, but slightly cupped. The right fundus was normal. Examination with the slit lamp revealed four unpigmented deposits on the posterior surface of the left cornea and bedewing of the corneal epithelium. The patient was given 2 per cent pilocarpine hydrochloride, and the tension dropped to 33 mm. within two hours. The tension returned to normal in two days, and the deposits disappeared within two weeks.

COMMENT

The importance of the recognition of this syndrome lies in its forming a link between the primary and the secondary glaucomas, since it cannot be classified in either category. For this reason, this group of cases assumes a significance far greater than is warranted by the low incidence of the syndrome.

A review of the literature reveals two papers dealing with this syndrome. Terrien and Veil[2] described a heterogenous group of cases to illustrate the importance of careful examination with the slit lamp in every case of glaucoma. Among them were 3 cases, perhaps 4, which belonged to this type, and only 1 of these was followed sufficiently long to permit observation of more than one attack. The authors did not attempt to classify these cases except to place them in the general category of secondary glaucomas. Kraupa described 4 similar cases and recognized that they represented a distinct clinical entity (1935).[1] He noted the relation between heterochromia and this type of glaucoma. He reasoned that the underlying pathologic mechanism of both types (with and without heterochromia) is in some way related to the sympathetic nervous system and called it "glaucoma allergicum" for want of a better name. Since it is generally accepted that the autonomic nervous system plays a role in all glaucomas, we felt that this name would not circumscribe this special group of cases. Moreover, Kraupa's title carries etiologic implications which we are not yet prepared to corroborate or to disprove. There is no article in the English literature dealing with this syndrome. Kronfeld, in one of his papers,[3] mentioned a group of "cases of acute elevation of intraocular pressure occurring simultaneously with mild recurrent cyclitis." He mentioned them only to exclude them from a general discussion of secondary glaucomas because, in his opinion, this condition represents "a clinical entity." Since he did not define them further, it is difficult for us to know whether he

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2. Terrien, F., and Veil, P.: Certain So-Called Primary Glaucomas, Bull. et mem. Soc. Franc. d'opht. **42**:349, 1929.

3. Kronfeld, P. C.: Gonioscopic Correlates of Responsiveness to Miotics, Arch. Ophth. **32**:447 (Dec.) 1944.

referred to the syndrome discussed here. Textbooks on ophthalomolgy, including Duke-Elder's,[4] do not separate this type, and the more recent papers[5] dealing with the over-all relation of glaucoma to cyclitis take no cognizance of the specific symptomatology and clinical behavior of this entity.

According to the generally accepted teaching, the findings of keratic precipitates or cells in the aqueous stamps a case of glaucoma as secondary to uveitis. Some authors even regard the presence of pigment dust on the posterior surface of the cornea[5] or the anterior surface of the lens[6] as evidence of associated uveal involvement. Since a large proportion of normal persons, especially in the older age group, show such precipitates, this criterion has been discarded by more recent observers.

We wish to emphasize that the presence of keratic precipitates is only one of several factors which have a bearing on the pathogenesis and clinical course of a specific case of ocular hypertension. The classification of a case as one of secondary glaucoma does not of itself help one in the management or the prognosis. It has been stated by a number of writers that glaucomas secondary to uveitis are extremely variable and that their course is unpredictable. We feel, therefore, that if a homogeneous group of cases can be segregated from the general class of secondary glaucomas, it represents a definite advance in knowledge of this poorly understood subject.

This leaves the over-all relation of glaucoma to iridocyclitis still unsolved. A few clues, however, presented themselves in the course of this study.

Two patients, who have been followed for fourteen and nineteen years, respectively, showed a combination of true primary glaucoma and iridocyclitis.

CASE 10.—A. M., a housewife aged 67, was first seen in 1933 with acute iridocyclitis of the left eye, which was followed the next day by a similar inflammation of the right eye. She improved under treatment with atropine and scopolamine, but the ocular tension remained elevated. The eyes became quiet, and the patient did not return to the office until two years later. At this time she had tension of 65 mm. in each eye and deep cupping of both disks. The right field was normal, but the left field showed pronounced nasal contraction.

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4. Duke-Elder, W. S.: Text-Book of Ophthalmology, St. Louis, C. V. Mosby Company, 1941, vol. 3, p. 3288.

5. *(a)* Malling, B.: Relationship Between Iridocyclitis and Glaucoma, Acta ophth. **1**:97, 1923. *(b)* Larson, H.: Relationship Between Iridocyclitis and Glaucoma, ibid. **1**:345, 1923. *(c)* Fralick, F. B.; Cooper, J. H., and Armstrong, R. C.: Uveitis with Secondary Glaucoma, Tr. Am. Acad. Ophth. **47**:92, 1942-1943. *(d)* Weekers, L.: Treatment of Ocular Hypertension Complicating Iridocyclitis, Arch. d'opht. **53**:166, 1936.

6. Risley, S. S.: Simple Glaucoma, Ann. Ophth. **23**:437, 1914.

The picture was that of chronic simple glaucoma without symptoms. An Elliot trephine operation on both eyes normalized the tension, and her status has remained unchanged to the present. The tension curve is shown in chart 3.

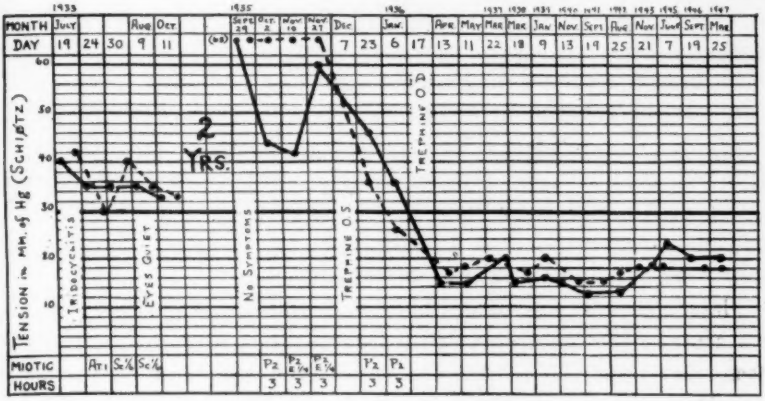

Chart 3 (case 10).—Tension curve for a patient with glaucoma simplex complicated by iridocyclitis in both eyes. *At.*$_1$ indicates atropine sulfate, 1 per cent; *Sc.* 1/6, scopolamine hydrobromide, 0.16+ per cent; *P*$_2$, pilocarpine hydrochloride, 2 per cent; *E*¼, physostigmine, salicylate, 0.25 per cent.

CASE 11.—M. N., a business man aged 64, was first seen in 1929 with an acute attack of iridocyclitis and hypertension in his left eye. The eye was intensely injected. A 2 plus aqueous flare and keratic precipitates were present. He gave a history of having seen colored halos intermittently for two years.

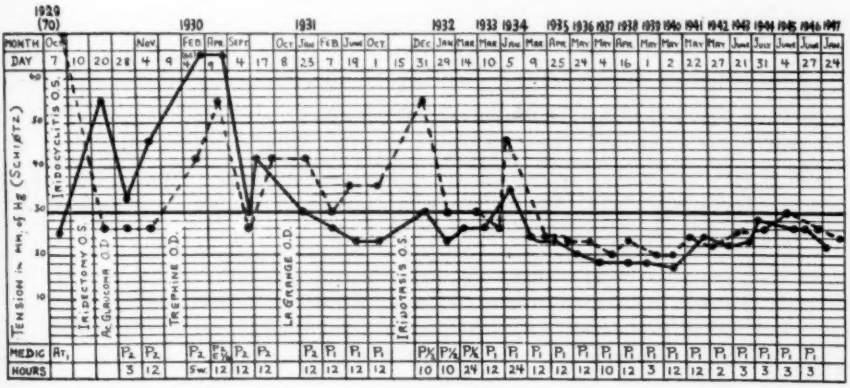

Chart 4 (case 11).—Tension curve for a patient with chronic congestive glaucoma complicated by iridocyclitis in the left eye. *At*$_1$ indicates atropine sulfate, 1 per cent; *P*$_2$, pilocarpine hydrochloride, 2 per cent; *E* 1/6, physostigmine salicylate, 0.16+ per cent; *P*$_1$, pilocarpine hydrochloride, 1 per cent; *P*½, pilocarpine hydrochloride, 0.5 per cent.

Since atropine did not control the attack, an iridectomy was performed one week later. Ten days after the operation, an attack of acute congestive glaucoma occurred in the other eye, without any manifestations of iridocyclitis. The tension at first responded to miotics but later rose again, and an Elliot trephination was performed. After a Lagrange sclerectomy on the right eye in 1930 and iridotasis on the left eye in 1931, tension, with the use of miotics, became relatively normal and has remained so up to the present time. The tension curve is shown in chart 4.

In these two cases a diagnosis of secondary glaucoma was originally made, but the subsequent course has given conclusive proof that the iridocyclitis was incidental to a primary glaucoma. The iridocyclitis may have acted as a precipitating factor, or the atropine used in treating the uveitis may have made the primary glaucoma manifest. It is important to guard against a hasty diagnosis of secondary glaucoma, on the basis of a brief period of observation.

These 2 cases (cases 10 and 11), which were uncovered only in retrospect after careful analysis of their course, illustrate the pitfalls in the present day approach to the problem of the relation of glaucoma to iridocyclitis and of iridocyclitis to glaucoma.

The following classification of glaucoma associated with iridocyclitis may prove helpful.

(1) Iridocyclitis occurring in a patient with primary glaucoma.
(2) Relatively mild cyclitis in which ocular hypertension occurs at the onset, or early in the course, of the disease.
   (a) Syndrome of recurrent glaucomatocyclitic crises.
   (b) Iridocyclitis without posterior synechias (or with old synechias) associated with the early appearance of ocular hypertension.
(3) True secondary glaucoma resulting from iridocyclitis.
   (a) Early stage, associated with plasmoid aqueous, active iridocyclitis and fresh posterior synechias.
   (b) Later stage, associated with structural changes in the filtration channels or with long-standing uveitis.

Other clues which have a bearing on the over-all relation of glaucoma to iridocyclitis may be derived from a careful interpretation of the features presented by the syndrome of glaucomatocyclitic crises, since this represents a true intermediate group between the primary and the secondary glaucomas. The following features relate this syndrome to secondary glaucoma:

1. Strict unilaterality of the ocular hypertension over many years of observation
2. The presence of cells in the aqueous and keratic precipitates during, and for a short time after, most attacks
3. The occurrence of glaucoma in the lighter-colored eye in 3 cases with heterochromia
4. Lack of uniformity in response to miotics and mydriatics

The following features relate it to the primary glaucomas:

1. In 3 out of 6 cases, pupillographic studies showed the type of curve usually found with primary glaucoma.

2. In all 6 cases the pupillographic responses were the same in the two eyes. This has been shown to be characteristic of unilateral primary glaucoma (Lowenstein and Schoenberg).

3. The attacks of ocular hypertension sometimes preceded the appearance of cyclitic signs by a day or two.

4. The severity of the glaucomatous attack was out of proportion to the cyclitic manifestations.

5. In 2 cases in this series primary glaucoma was present in another member of the family. This ratio is in line with the percentage of cases of hereditary glaucoma found by us in a study of 400 cases of primary glaucoma.[8]

6. Individual attacks might occur without any keratic precipitates or cells in the aqueous, although previous episodes were accompanied with these changes. In this connection, we wish to report a case which puzzled not only us but other ophthalmologists as well, and which may be understood better in the light of the present concept.

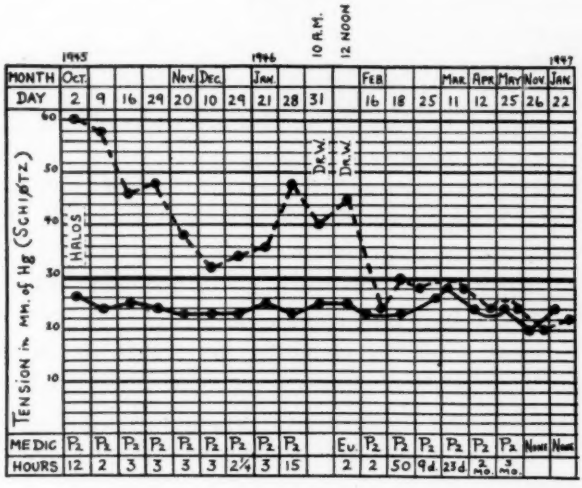

Chart 5 (case 12).—Tension curve for a patient with glaucoma (self limited) in the left eye. P_2 indicates pilocarpine hydrochloride, 2 per cent; *Eu*, eucatropine hydrochloride, 5 per cent.

CASE 12.—M. G., a housewife aged 49, was first seen by us on Oct. 2, 1945. She had had recurrent blurred vision and noted rainbows in her left eye, especially at night, for two weeks. Tonometric readings were 26 mm. in the right eye and 60 mm. in the left eye. Corrected vision was 20/30 in the right eye and 20/25 in the left eye. The pupils were equal. The irises were of the same color. Examination with the slit lamp failed to show any cells or deposits. Both anterior chambers were of normal depth, but the angles were moderately narrow. In spite of the use of 2 per cent pilocarpine hydrochloride, the tension remained between 45 and 60 mm. for nearly two months, after

7. Lowenstein, O., and Schoenberg, M. J.: Pupillary Reactions of the Seemingly Unaffected Eye in Clinically Unilateral Simple Glaucoma: Pupillographic Contributions to Diagnosis of Glaucoma in Preclinical Stage, Arch. Ophth. **31**:392 (May) 1944.

8. Posner, A., and Schlossman, A.: Development of Changes in Visual Fields Associated with Glaucoma, Arch. Ophth., to be published.

which it dropped to 30 mm. Vision in the right eye improved to 20/15. The fields showed no change. On November 9 the patient had, for the first time, an attack of bronchial asthma and a temperature of 99.8 F. She had a family history of allergy.

On Jan. 29, 1946, the tension rose again to 49 mm. in the left eye, and she complained of seeing a black circle and dots in the central field of that eye. Another ophthalmologist dilated her left pupil with eucatropine hydrochloride U.S.P., which raised the tension only by 5 mm. With mydriasis [illegible] line surrounded by dusty opacities was seen in the vitreous adjacent to the retina in the macular zone. No focus of choroiditis was present. Surgical intervention was suggested by this, and still another, prominent ophthalmologist, the latter making the diagnosis of primary glaucoma. Operation was temporarily deferred. On Feb. 16, 1946, the tension was down to 24 mm., and the patient complained of severe, sharp pain in her eye after use of the miotic. All medication was discontinued. The pain subsided, and the tension has remained normal and equal in the eyes up to the time of this report. The opacities in the vitreous have since disappeared. Pupillographic studies on March 24, 1946, six weeks after discontinuation of miotics, revealed a bilateral curve similar to that found in cases of primary glaucoma (chart 5).

This case of self-limited unilateral glaucoma of the congestive type, which was regarded as primary at first, shows several obvious points of similarity to the syndrome of glaucomatocyclitic crises. It differs from the latter in the absence of signs of cyclitis. However, several opacities in the vitreous, which may well have been cells or clumps of cells, were observed adjacent to the retina without any visible choroiditis. These appeared during the course of the glaucoma and disappeared after subsidence of the hypertension.

Like the pathogenesis of glaucoma in general, the mechanism involved in the production of glaucomatocyclitic crises is obscure. However, we shall venture to advance a hypothesis based, to a certain extent, on established physiologic principles. It is our impression that this syndrome is engendered by a central disturbance in the hypothalamus, superimposed on a labile peripheral autonomic nervous system. The central factor is expressed by the bilaterality of the pupillographic findings (even when the curve is not the same as that found in cases of primary glaucoma) and by the association with hypertensive vascular disease, migraine and allergies, and with fever in 1 case. The peripheral factor was evidenced by the unilaterality of the disease, anisocoria, heterochromia and homolateral urticarial manifestations in 2 cases. It is possible, however, that a unilateral disease picture, such as this is, may be explained entirely on the basis of a central disturbance in the hypothalamus.

The fact that the disease in this group of cases was unilateral does not exclude the possibility, on the one hand, that certain cases of bilateral uveitis with glaucoma in which the latter is out of proportion to the former, and, on the other, some cases of glaucoma which pass as

primary only because of the absence of keratic precipitates, may also be related to this entity.

Treatment should be administered cautiously. Pilocarpine hydrochloride may be used in low concentrations of 0.5 to 2 per cent. Phenylephrine hydrochloride, 10 per cent, or epinephrine bitartrate, 2 per cent, may be tried; but the patient should be under observation for a few hours. Physostigmine, neostigmine and occasionally even pilocarpine may cause acute discomfort and redness of the eye. We were loath to use di-isopropyl fluorophosphate in this group of cases. Although the drug proved extremely beneficial in some of our cases of refractory glaucoma, it gave rise to severe discomfort in a few patients of the younger group.[9] In a case of acute glaucoma with minimal subjective and objective signs, it is advisable to use medication cautiously until the nature of the disease becomes evident. Surgical intervention is contraindicated, since the course is not influenced by it. Paracentesis has been reported to be of value in relieving an acute attack.[2]

SUMMARY

Nine cases, forming a homogeneous group which represents a type of glaucoma intermediate between primary and secondary glaucoma, are described.

It is proposed to call this condition a syndrome of glaucomatocyclitic crises, to distinguish it from primary glaucoma, on the one hand, and secondary glaucoma, on the other.

A tentative hypothesis is advanced which relates this syndrome to a disturbance of the central and the peripheral autonomic nervous system.

Treatment should be confined to the use of low concentrations of pilocarpine hydrochloride.

A classification of glaucoma associated with iridocyclitis is presented.

667 Madison Avenue.

A few of these cases were originally those of the late Dr. Mark J. Schoenberg. His carefully kept records and detailed notes helped us greatly in the preparation of this paper.

The pupillographic studies were made by Dr. Otto Lowenstein. All tension readings refer to the 1924 Schiotz graph unless otherwise stated.

9. A patient, aged 57, who is subject to recurring attacks of unilateral glaucoma without congestive or cyclitic signs, received 1 drop of di-isopropyl fluorophosphate ("DFP"). This was followed by marked reduction of tension. However, extreme discomfort, injection of the bulbar conjunctiva and pain when he attempted to read lasted for two weeks and was only temporarily relieved by homatropine.

DISCUSSION

DR. L. VON SALLMANN, New York: It was of great benefit to us to have Dr. Posner and Dr. Schlossman direct our attention to a type of unilateral glaucoma so far scarcely considered or recognized as a definite syndrome. Such recurrent attacks of increased intraocular tension with transient cellular and larger deposits on the cornea are usually considered of borderline type, and treatment is rather arbitrary, depending on the ophthalmologist's intuition. From the authors' description, it is evident that this syndrome can be fairly well distinguished from typical primary glaucoma with a few deposits on the cornea, from primary glaucoma with superimposed cyclitis unrelated to the glaucoma, from secondary cyclitic glaucoma and from the so-called sympathetic glaucoma of Streiff, with and without heterochromia.

It may not be easy to make this distinction in an isolated case, since similar signs and symptoms are common to other groups, and since, as we have learned from Posner and Schlossman's paper, close study of the course of the disease over long periods is necessary to obtain conclusive diagnostic data. However, the observations presented here, together with those in Kraupa's and a few other cases reported in the literature, round out the picture and strengthen the impression that the disease represents an entity.

Posner added to the general symptomatology of the disease the results of the pupillographic examinations and concluded from them, on the basis of Otto Lowenstein's work, that the sympathetic center in the diencephalon was involved. I must leave it to the experts in this field to evaluate and to interpret the pupillographic curves. There is no reason to doubt the correctness of this interpretation. Nevertheless, the question may be raised whether, in view of the unilaterality of the lesion, a disorder in the subordinate ciliospinal center of Budge can be completely disregarded. In 3 of Posner's cases, in 1 of Passow's cases and in several of Kraupa's series there were varying degrees of heterochromia. Heterochromia, especially complicated heterochromia, was pathogenetically related by Passow, and recently by Appel and Leo Hess, to Bremer's status dysraphicus, which is said to be due to a congenital anomaly in the cervical area of the spinal cord. I believe that the authors' cases were not examined from this neurologic standpoint.

In addition to the hypothalamic disturbance, Posner assumes the coexistence of a peripherally operating mechanism, such as a labile peripheral autonomic system; this factor must be present unilaterally. There seems to be a considerable range of alternative explanations and speculations. One could assume that the functions of the terminal nerves or the capillary motor response of other intraocular mechanisms of regulation are at fault in the one eye. In view of the presence of infective foci and the strong allergic reactions of some of the patients, the question arises whether an antigen-antibody reaction or a toxic factor could not be responsible for the onset of the periodic attacks in a disposed eye. That is, the cells in the aqueous and the precipitates on the cornea could be the expression of a transient, low grade inflammation rather than of a primarily nervous disturbance.

What further studies may reveal on the relation between disorders of the sympathetic centers and between the centers and a peripheral mechanism remains to be seen. At present, it seems likely that a transient increase in the permeability of the ciliary capillaries is the most important single peripheral factor which has a bearing on the development of the recurrent attacks. In the last year studies were conducted in the Knapp Laboratory on an experimental glaucoma induced by increased permeability of the ciliary capillaries. Various therapeutic approaches were studied on experimental animals. The effects of adrenergic drugs, of posterior pituitary injection U. S. P,. of substances acting on the intracellular cement, such as calcium ions and adrenal cortex hormone, and of a series of histamine antagonists were tested, and promising results were obtained in respect both to the reduction of increased permeability of intraocular capillaries and the lowering of intraocular tension. There is some hope that one or another of these therapeutic measures will be of help in the glaucomatocyclitic crises described by Posner and Schlossman.

CONGENITAL GROUPED PIGMENTATION OF THE RETINA

Report of Two Cases

PAUL TOWER, M.D.
LOS ANGELES

Congenital grouped pigmentation of the retina is a rarely encountered condition; Stephenson [1] found only 3 instances of this anomaly in a series of 2,400 examinations, while Blake [2] noted not more than 7 cases of this kind in twelve years of ophthalmologic practice. The clinical picture of grouped pigmentation, as well as the characteristic features distinguishing it from abnormal multiplication due to a progressive pathologic process, were excellently described by Stephenson.

> The changes which occupy a sector-like portion of the fundus, consist of groups made up of black to dark chocolate brown spots, which, as seen by the direct method, range in size from 0.5 to 2 mm., or more; in general terms it may be said that the farther away the spots lie from the optic disk the larger they become.

This specific hyperplasia of the pigmented cells of the retina is listed in the literature under various names: congenital pigmentation of the retina, melanosis retinae and congenital pigmented plaques of the retina. The term "nevoid pigmentation of the fundus," which is also sometimes used, is misleading, as nevoid cells have never been encountered in this condition.

Illustrations of grouped pigmentation of the retina were published as early as 1868; yet the true character of this anomaly was not recognized at that time, and the condition was erroneously described as an unusual form of progressive pigmentary degeneration, similar in many respects to retinitis pigmentosa. While most of the ophthalmologic textbooks fail to mention grouped pigmentation of the retina, an example appears in Bedell's [3] atlas of photographs of the fundus oculi (1929); in that case, a group of four round spots of retinal pigment can be discerned beneath one of the radicles of the temporal branch of the inferior

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1. Stephenson, S.: A Peculiar Form of Retinal Pigmentation, Tr. Ophth. Soc. U. Kingdom **11**:77, 1891.

2. Blake, E. M.: Congenital Grouped Pigmentation of the Retina, Tr. Am. Ophth. Soc., 1926, p. 223.

3. Bedell, A. J.: Photographs of the Fundus Oculi: A Photographic Study of Normal and Pathological Changes Seen with the Ophthalmoscope, Philadelphia, F. A. Davis Company, 1929, vol. 2, p. 274.

portion of the vena centralis retinae. The patient's vision in this eye was reported as 20/20. Three cases were described by Mann[4] in 1932. The single case reported by Perera[5] in 1939 is accompanied with a photograph presenting the arrangement of pigment which is typical of this condition, as well as with a description of the characteristic signs of grouped pigmentaton. The necessity of careful differentiation of this anomaly and pigmentation due to hemorrhage, or other pathologic processes was stressed by Casanovas,[6] in commenting on an additional case in 1945.

Little is known about the pathologic process in grouped pigmentation. No satisfactory explanation appears to have been given for the typical feature of this anomaly: the appearance of dark spots in a characteristic arrangement within certain segments of the retina, as distinguished from the continuous layer of normal coloring matter encountered in the inner portion of the hexagonal columnar epithelial cells forming the stratum pigmenti retinae. Collins and Mayou[7] gave a brief description of grouped pigmentation on the basis of microscopic observations. Sir Herbert Parsons,[8] in an earlier pathologic study, encountered within the retina a number of deeply pigmented epithelial cells. Some of these were surrounded by nodules of hyaline matter, closely resembling the transparent substance of the lamina basalis of the choroid. He assumed that the anomaly of grouped pigmentation could be traced to irregularities in the evolution of the two layers of the retina within the secondary optic vesicle: Whenever rods and cones fail to develop in Jacob's membrane, empty spaces occur into which the pigmented epithelial cells of the outer stratum will migrate. Collections of such supernumerary cells containing a deposit of coloring matter produce the typical plaques of congenital grouped pigmentation. Ida Mann[9] stated that this developmental abnormality may be caused by an atypical process in the differentiation of the optic cup during the embryonic stage. Either irregular chromatosis may occur within groups of plastids in the inner stratum, or the outer stratum, which normally persists as a single cellular layer, may undergo localized proliferation.

4. Mann, W. A.: Grouped Pigmentation of the Retina, Arch. Ophth. **8**:66 (July) 1932.

5. Perera, C. A.: Congenital Grouped Pigmentation of the Retina, Arch. Ophth. **21**:108 (Jan.) 1939.

6. Casanovas J.: Grouped Pigmentation of the Retina, Arch. Soc. oftal. hispanoam. **5**:129 (Feb.) 1945.

7. Collins, E. T., and Mayou, M. S.: Pathology and Bacteriology of the Eye, ed. 2, Philadelphia, P. Blakiston's Son & Co., 1925, p. 27.

8. Parsons, J. H.: Anomalies of Pigmentation, Tr. Cong. internat. d'opht., 1904, p. 152.

9. Mann, I.: Developmental Abnormalities of the Eye, New York, The Macmillan Company, 1937, pp. 153-154.

Two cases of grouped pigmentation of the retina are reported, one of which appears to be of special interest, as the observations in this instance may permit certain conclusions relative to the developmental mechanism responsible for this rare anomaly.

REPORT OF CASES

CASE 1.—H. F., a white woman aged 30, was referred because of a suspected pathologic condition of the fundus. Inspection of the exterior of the eyes failed to reveal any significant data. Refraction demonstrated bilateral visual acuity of 20/20, without correction. Vision in the fields peripheral to the point of fixation was normal bilaterally, and no scotomas occurred in the center of the visual field. On ophthalmoscopic examination, both fundi presented a somewhat tassellated appearance; but the arteries were normal, and the optic disk was well defined in both eyes. In the right fundus, in a sector of the nasal half of the retina, several groups

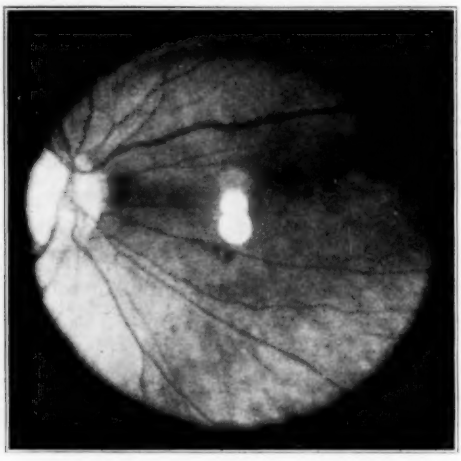

Fig. 1 (case 1).—The fundus of the right eye is marked by groups of pigmented spots occupying an area nasal to the disk.

of pigmented spots, slightly varying in size and shape, but all of dark gray color, were encountered (fig. 1). These patches occupied a position which, even though it was deeper than the pigmented layer of the retina, appeared to be above the inner surface of the choroid. Otherwise, the fundus of the right eye was normal. No chromatism was found in the fundus of the left eye.

CASE 2.—M. M., a white boy aged 12 years, was examined for correction of refractive errors. Inspection of the exterior of the eyes failed to reveal any significant data. Refraction demonstrated the visual acuity as 20/20 with a correction of +0.50 cyl., axis 175, for the right eye, and +0.50 cyl., axis 180, for the left eye. Vision in the fields peripheral to the point of fixation was normal bilaterally, and no scotomas occurred in the center of the visual field. No muscular insufficiency was encountered, and the media were clear. Ophthalmoscopic study revealed numerous pigmented spots in the lower portion of the retina of the right eye (fig. 2). These patches of a chocolate brown color were arranged in groups, but larger spots were encountered at the periphery than close to the optic disk. In the lower portion of

the left retina, there appeared pigmented spots of a color similar to that in the right eye. But in the left fundus the patches were more numerous and larger; they were also assembled into groups, and those at the periphery were much more extended than those closer to the optic disk. On this side, however, the typical arrangement of these spots into only one sector of the retina was still more obvious (fig. 2B). Bilaterally, the patches occupied a position which, even though deeper

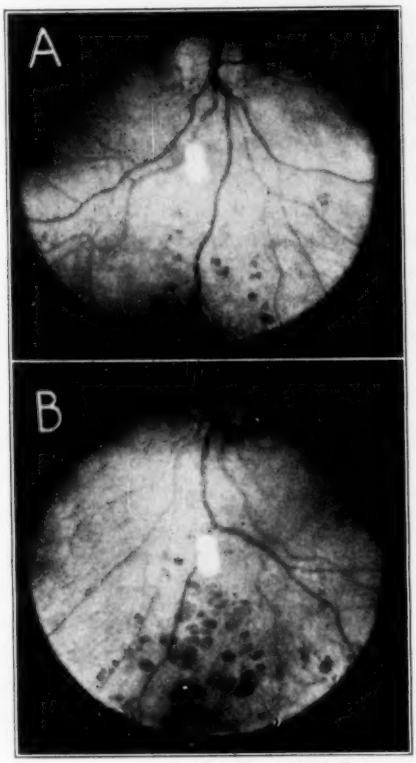

Fig. 2 (case 2).—(*A*) The fundus of the right eye is marked by pigment deposits occupying the lower portion of the retina. (*B*) The fundus of the left eye is marked by pigmented plaques characteristically arranged in a triangular sector of the lower portion of the retina.

than the pigmented layer of the retina, appeared to remain above the inner surface of the choroid.

COMMENT

The similarities between these 2 typical cases of grouped pigmentation are clearly evident, even though in the first instance the involvement was only unilateral and the pigmented spots were neither as frequent nor as dark as in the second case. The family history failed to reveal the appearance of any comparable condition within the family of either patient,

nor was there any evidence of consanguinity. There seems to exist, therefore, no valid foundation for an assumption of the hereditary origin of this rare anomaly. It is of note, furthermore, that neither of the patients presented deformities in any other part of the body.

The diagnosis of grouped pigmentation should be based on the following pathognomonic symptoms: no defect in vision referable to the condition, and normal visual fields. The pigmented patches are typically grouped within one triangular sector of the retina; this arrangement may be more or less clearly apparent in the individual case. Only in rare instances will the area marked by chromatism extend to include the macula lutea. Generally, the pigmented deposits can be identified as situated at a deeper level than the retinal structures, but still distinguishably above the lamina basalis of the choroid. No evidence of further congenital anomalies is encountered in patients presenting grouped pigmentation of the retina, and rarely, if ever, will a similar condition be detected among other members of the patient's family. Congenital grouped pigmentation is, finally, not progressive.

Even though other pathologic processes affecting the fundus of the eye may at first glance seem to produce a similar appearance on the retina, the differential diagnosis of grouped pigmentation should not prove difficult on the basis of the enumerated signs.

Of the 2 cases reported here, the second would appear to be of particular interest. In this case, the arrangement of the groups of pigmented spots in a single sector in the lower portion of the retina—the apex of which points toward the disk, or is identical with it—becomes clearly evident. Yet this triangular region of the retina to which the anomaly of grouped pigmentation seems to be restricted in typical cases corresponds closely to the zone of the choroid to which the occurrence of coloboma is usually limited. It is not intended to enter into a detailed discussion of coloboma at this point. But the obvious similarity of the area of involvement in the two developmental abnormalities may possibly indicate a deeper than merely topographic relation between grouped pigmentation of the retina and coloboma of the choroid.

Coloboma can be traced to the persistence of the choroidal fissure of the optic cup and the optic stalk, which usually closes during the seventh week of fetal life. Coloboma of the choroid frequently produces scotoma of the retina, a condition which is rarely, if ever, concomitant with grouped pigmentation. But if Parsons'[8] hypothesis of the probable cause of congenital grouped pigmentation is accepted and the development of supernumerary deposits of coloring matter is traced to a localized defect in the development of the layer of rods and cones, then the topographic analogy between the congenital anomalies of grouped pigmentation of the retina and coloboma suggest a similar etiologic factor in the two conditions. Conceivably, the anomalous accumulation of pigment in Jacob's

membrane may be due to an irregularity in the occlusion of the choroidal fissure, different, of course, from that leading to coloboma. Or, on the other hand, some other pathologic process during the patency of this fetal cleft may result in a disturbance of the development of the different strata of the retina. At present, no additional evidence is available which would help in substantiating this theory of the possible causes responsible for the occurrence of grouped pigmentation of the retina. Yet the localization of the pigmentary deposits in a specific sector of the fundus, so clearly evident in the second case presented here, is a factor which should be taken into consideration in any future study of the cause of this congenital anomaly.

SUMMARY

Two cases of congenital grouped pigmentation of the retina are presented.

The literature on this congenital anomaly, especially that relating to its pathology, is reviewed.

The necessity of differential diagnosis from other conditions affecting the fundus of the eye is stressed.

The typical arrangement of the deposits of coloring matter in a triangular sector of the inferior portion of the retina suggests that this anomaly may have a cause similar to that of coloboma of the choroid, and that it may be possible to trace it to irregularities in the closure of the choroidal fissure.

610 South Broadway (14).

CRESCENTIC DEFORMITIES OF THE LID MARGIN

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NEW YORK

Crescentic (lunate) dehiscences of the lid margin are deformities in which there is absence of an appreciable portion of the border of the lid, but the lesion is shallow and rarely extends beyond the tarsus. Although the loss of tissue is not great, the deformity is usually unsightly and, if the upper lid is involved, leaves a large area of cornea exposed (fig. 2*A*). While reconstruction of this defect does not present a major problem, careful handling is required to get a good cosmetic result. Of several methods tried, the technic to be described was found to be the simplest and to yield the best results in a series of 14 cases. Photographs from an illustrative case are presented (fig. 2).

TECHNIC

The involved portion of the lid is split into a skin-muscle and a tarsoconjunctival layer, the dissection being made sufficiently wide to mobilize both layers thoroughly. All scar tissue is carefully resected. The opposing lid edge is freshened and also split into its two layers, but only to a depth of about 2 mm. (fig. 1*A*, broken lines). The tarsoconjunctival layers of the two lids are united by a 00000 braided black silk (running) suture, anchored at both ends. The skin-muscle layer of the injured lid will now retract, leaving an area of raw tarsal surface exposed (fig. 1*B*). If necessary, a mattress suture is passed through the uninvolved portion of the lid margins to immobilize them (fig. 1*B*).

A free graft, cut to pattern, is then taken from the brow. This includes about 4 mm. of brow hair to replace the lost cilia of the lid margin and some clear skin to make up for the rest of the lost cutaneous tissue of the lid (fig. 1*B*, broken oval). This graft should be cut about a third larger than the recipient site to allow for shrinkage. The graft is sewed into place with 00000 braided black silk interrupted sutures. The donor site is closed with 0000 mild chromic surgical gut subcuticula sutures and 0000 braided black silk skin sutures (figs. 1*C* and 2 *B*). The site of operation is covered with perforated oiled silk or "cilkloid" and a firm pressure dressing applied. It is not necessary to patch the fellow eye. The dressing is removed on the seventh day; the area is cleansed; the brow sutures are removed, and the pressure dressing is reapplied for five days longer. By this time the graft has "taken," and the sutures are removed. The eye is patched daily for a few more days until healing is complete, at which time dressings are discontinued. The lids are separated four weeks later and the edges are allowed to epithelize. The lid will be somewhat thickened for a month or so and will then assume a normal appearance. Cilia should begin to reappear six to eight weeks after operation (fig. 2*C*).

From the Department of Ophthalmology, New York University School of Medicine.

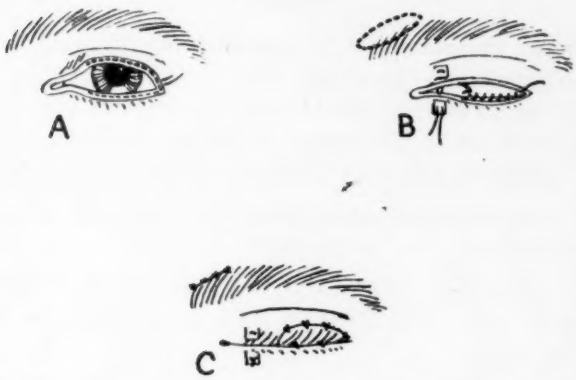

Fig. 1.—Technic of repair of crescentic deformity of the lid margin. See text for explanation.

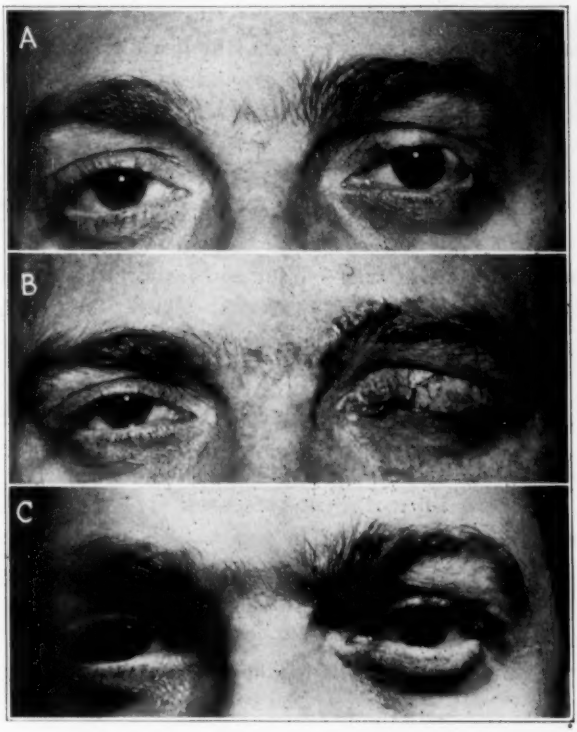

Fig. 2.—*A*, crescentic dehiscence of the left upper lid, with abnormal exposure of the cornea; *B*, one week after repair, with donor site healed and graft "taking" well; *C*, ten weeks after repair, with the corneas showing qual exposure. Note the normal lid line and good growth of transplanted lashes. The donor site is well covered.

COMMENT

In another communication,[1] a method of repairing these lunate marginal deformities was described. This involved two stages: (*a*) reconstruction of the lid margin and (*b*) lash grafting, at a later stage. The method proposed here is preferable, for several reasons:

1. The patient is subjected to only one operative procedure.

2. Less surgical intervention means less scarring and therefore a better cosmetic result.

3. It is believed that this type of lash graft is more certain to "take" than the usual 3 mm. wide, hair-bearing graft planted in a trough near the lid margin.

4. The lash graft is closer to the lid margin and hence gives a more natural appearance.

In taking these grafts, it is probably preferable to use tissue from the lower part of the brow and the skin below it, for this matches the skin of the lid more closely in color and texture. If the socket had been anophthalmic in the case presented here, the graft would have been taken from the lower part of the left eyebrow and the skin below it. However, in that case the direction of the transplanted lashes would have been down and nasal. While this does not matter in an anophthalmic orbit, the normal eye might have been subjected to some trichiasis, since it is difficult to change the direction of hair growth. Hence, the graft was taken as shown.

Skin from above the brow is thicker and somewhat paler than the skin below the brow. But while it is a trifle more difficult to handle, experience shows that the "take" is as certain, and after several weeks the cosmetic result is about as good.

SUMMARY

A method of simultaneous lash grafting and reconstruction of crescentic deformities of the lid margin is presented.

63 East Seventy-Fifth Street (21).

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1. Fox, S. A.: Some Methods of Lid Repair and Reconstruction, Am. J. Ophth. **29**:452 (April) 1946.

Mr. Herbert M. Kraus assisted in drawings of the technic.

COTTON SUTURES IN OPHTHALMIC SURGERY

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ROCHESTER, MINN.

During the past seven years several reports [1] concerning the use of cotton thread as a suture material have appeared in the literature. These reports were made by general surgeons and were based on the use of cotton sutures in more than 3,000 cases. In most instances the general surgeons were favorably impressed with the use of cotton for suturing certain types of wounds. No reports on the use of cotton as a suture material in clinical ophthalmology were made in a similar seven-year period. Berens and Romaine [2] included cotton thread in their report on the comparative value of sutures employed in surgical procedures on the extraocular muscles, but their experimental work was carried out on rabbits. In the military service I used cotton as a suture material in approximately 50 operations on the eye. It seems to possess features that make it applicable to certain types of ophthalmic surgery.

Cotton fiber, a cellulose material, has a natural twist which facilitates its being spun into thread. Because of this natural twist of the individual cotton fiber, the finished thread is very compact in structure. Fraying of cotton thread is negligible, and the natural twist facilitates the tying of a knot. In spite of its compactness, cotton thread still possesses a high

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From the Section on Ophthalmology, the Mayo Clinic.

Read at the meeting of the Minnesota Academy of Ophthalmology and Otolaryngology, Rochester, Minn., May 16, 1947.

1. (*a*) Meade, W. H., and Ochsner, A.: The Relative Value of Catgut, Silk, Linen, and Cotton as Suture Material, Surgery **7**:485-514 (April) 1940. (*b*) Meade, W. H., and Long, C. H.: The Use of Cotton as a Suture Material, with Particular Reference to Its Clinical Application, J. A. M. A. **117**:2140-2143 (Dec. 20) 1941. (*c*) Thorek, P.: Five Years' Experience with Spool Cotton as Suture Material: Routine Use in over One Thousand Operations, Am. J. Surg. **71**:652-656 (May) 1946. (*d*) Kanne, W. P., and Smith, W. E.: Clinical Observations on the Use of Cotton as a Suture Material, Ohio State M. J. **41**:625-627 (July) 1945. (*e*) Floyd, J. R., and Brockbank, M. J.: Spool Cotton as Suture Material, Surgery **16**:403-406 (Sept.) 1944. (*f*) Hyde, T. L.: Cotton Surgical Suture Material, ibid. **16**:407-415 (Sept.) 1944.

2. Berens, C., and Romaine, H. H.: A Comparative Study of Sutures Employed in Surgery of the Extraocular Muscles, Am. J. Ophth. **29**:1126-1134 (Sept.) 1946.

friction coefficient, so that a knot or hitch shows no tendency to slip even though the ends of the thread are cut short. From the standpoint of the ease with which it can be tied, the absence of slipping and the smallness of the resulting knot, cotton thread is preferable to chromic surgical gut, plain surgical gut or silk.

Commercially, cotton thread is often treated with chemicals in order to increase its tensile strength. Mercerized cotton is thread that has been immersed in sodium hydroxide. Quilting cotton is thread that has been immersed in starch. Spool cotton, or ordinary sewing cotton, has little or no chemical impregnated in the thread. The irritating effect of chemically treated cotton on body tissues has not been determined experimentally, but clinically mercerized and quilting cotton do not seem to possess distinct advantages over spool cotton. The tensile strength of spool cotton is increased from 10 to 15 per cent [1a b] by wet sterilization, whereas the tensile strength of silk is [1b f] decreased by similar sterilization. Berens and Romaine [2] estimated the tensile strength of a strand of 000 cotton to be between 2 and 3 pounds (0.9 and 1.3 Kg.). This tensile strength of cotton is about equal to that of chromic surgical gut, a little greater than that of silk and about twice as great as that of plain surgical gut, when similar-sized threads are compared. From the standpoint of tensile strength, cotton thread compares well with other suture material.

Cotton is a relatively inert substance, as judged by the response of the body tissue to its presence. The natural twist of the cotton fiber and the compactness of the finished thread make the suture almost impervious to infiltration with cells or body fluids, so that the tensile strength of the suture is preserved. This feature is in striking contrast to the behavior of surgical gut, in which the suture is weakened in direct proportion to the fluid it absorbs and the cellular reaction that it incites. Even silk tends to fray and lose its tensile strength because of the tendency of cellular elements to migrate along the individual strands and of fluid to reach the center of the thread. This feature of cotton makes it the suture material of choice in the presence of infected wounds according to reports [1a c] in the literature.

The tissue reaction that is incited by cotton consists in fibroblastic proliferation and a slight lymphocytic response. The fibroblastic response, and, in reality, healing, occur earlier with cotton than with silk or surgical gut.[1a] The fibroblasts and lymphocytes seem to engulf the cotton suture and, in the initial phases of wound healing, surround the cotton thread like a cuff.[2] Berens and Romaine [2] performed recessions and resections with cotton sutures on the eyes of a series of rabbits and made microscopic studies of wound healing at intervals of twenty, forty and sixty days after operation. Twenty days after operation they noted the fibroblastic cuff around the suture. Forty days after operation they observed "fibrous tissue replacement of suture." At the end of sixty days they noted fibrous

tissue but no evidence of the suture. Because cotton has been considered to belong to the nonabsorbable group of suture materials, it has rightly been considered to possess the danger of any retained foreign body; but, in view of the studies of Berens and Romaine,[2] perhaps it should be thought of as "relatively nonabsorbable." In 1 instance I had the opportunity to dissect an eye in which I had buried a cotton suture in the sclera near the limbus about four months previously. Grossly, I was unable to find the cotton suture. Even though the suture is a potential foreign body for at least a portion of the postoperative period, this disadvantage is somewhat modified by the minimal tissue response that is incited by cotton. Meade and Ochsner [1a] favored cotton over any other suture material from the standpoint of the least postoperative reaction of tissue and the earliest healing. With their statement I agree.

I first used cotton as a suture material in the so-called Mules-Dimitry operation, in which some type of implant is inserted into the scleral shell. This operation is often followed by intense postoperative edema, slipping or sloughing of the buried suture, gaping of the edges of the scleral wound and ultimate extrusion of the implant. With cotton sutures, I found there were less postoperative edema, no extrusion of the implant and earlier healing than with surgical gut or silk.

Next, I tried cotton sutures in the repair of wounds of the eyelids and margins of the eyelids. Where the wound had produced a defect in the margin of the eyelid and considerable loss of tissue substance, I inserted cotton sutures in the tarsal plate and was able to coapt the edges of the wound, even under considerable tension. With silk sutures there seemed to be a greater tendency of the suture line in the tarsus to spread. With surgical gut, infection and sloughing of the tarsus were common. Where it was necessary to repair a defect in the eyelid with some type of sliding flap, cotton sutures were placed in the subcutaneous tissues. This measure assured adequate tension and made it possible to insert fewer sutures in the superficial portion of the skin.

In recessions with scleral fixation and in resections on the extraocular muscles, I have used cotton sutures without complications. In these operations, the cotton sutures were buried and the overlying conjunctiva was closed with silk. The postoperative tissue reaction was less; the patients became ambulatory sooner, and muscle exercises could be started earlier than after similar operations in which surgical gut sutures were employed.

In dacryocystorhinostomy procedures I have utilized cotton thread for sewing the mucosa of the lacrimal sac to the nasal mucous membrane. I have not found that cotton is of any particular advantage over other types of suture material in the average case in which this operation is required. Theoretically, cotton might have advantages over other suture material in those cases in which purulent dacryocystitis has occurred

previously or in which gross contamination of the operative wound is likely.

In perforating wounds of the globe involving the region of the limbus and ciliary body, I have inserted cotton sutures in the sclera to prevent gaping. The inertness of the cotton fiber and the small knots that are possible would seem to recommend the cotton suture for these occasions.

I have had no experience with the use of cotton sutures in cataract operations or in the so-called tucking operations on the extraocular muscles. In some of the operative procedures designed for the correction of ptosis, cotton sutures might be used. I think this suture material might also be utilized in the muscle transplantations for paralytic strabismus.

In practically all cases in which I have used cotton, I have inserted it as an interrupted suture and have allowed it to remain in the tissues. For closure of surface wounds, I feel that black silk is preferable to cotton because it is more visible and more easily removed.

The ordinary commercial spool cotton in sizes 60 and 80 seems applicable to the demands of ocular surgery. Number 60 cotton thread is comparable in diameter to 0000 surgical gut U. S. P. Since manufacture of spool cotton is not well standardized, thread of similar diameters obtained from different sources will vary in tensile strength.

Since I was accustomed to using silk and surgical gut, I found cotton hard to work with at first. It is very limp, and it tends to stick to all objects and tissues in the operative field. It is not elastic, and it will break readily if tension is too rapidly placed on the thread during the tying of the knot. This is its chief disadvantage. One should be careful not to use too large a thread, for the suture will probably slough. One should remember that it has a high tensile strength, so that a small diameter of thread is sufficient.

SUMMARY

Cotton fiber is an inert material with a natural twist which can be tied into small, stabile knots with a high tensile strength, yet incites early healing but with little undesirable tissue response. These characteristics are features that might be considered in the possible use of cotton as a suture material in ophthalmic surgery.

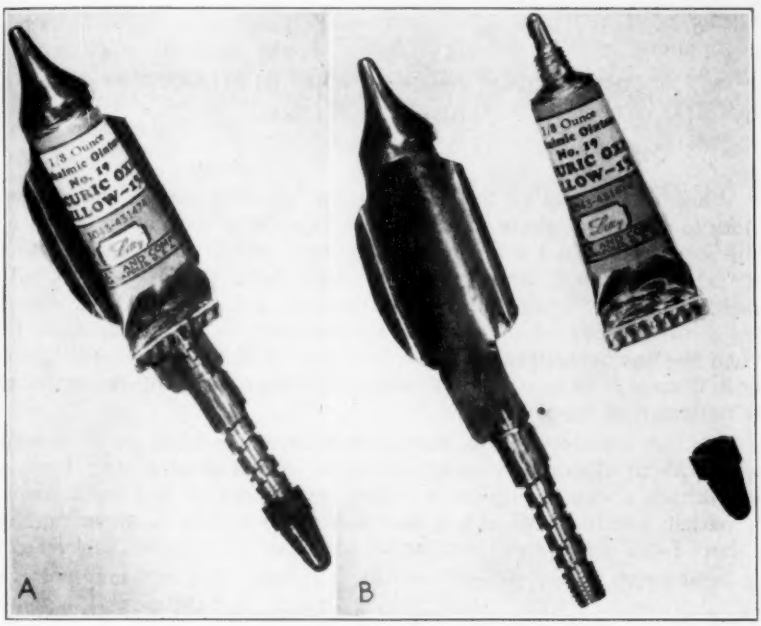
The Mayo Clinic.

Clinical Notes

EYE OINTMENT DISPENSER

R. TOWNLEY PATON, M.D.
NEW YORK

The danger of contamination from the tips of ointment tubes has long been recognized, and several substitute methods have been employed. None of these methods, however, has proved entirely satisfactory, and for this reason the metal container shown in the illustration was devised.



A, eye ointment dispenser with tube in position. The tube cap has been screwed on the end of the ointment dispenser. *B*, tube and cap of ointment dispenser.

Sterile glass or plastic rods for the application of ointment to eyes have two distinct disadvantages: 1. The method is cumbersome because of the changes in the viscosity of the ointment. During the summer months scarcely any ointment will adhere to the glass rod, while in the winter months and at cold temperatures too much ointment adheres to the rod. 2. The use of glass rods may be traumatizing to the sensitive eye.

Sterilization of the tubes is not practical, especially in office practice and in wards, where they must be resterilized after each application.

A metal nozzle or glass tip screwed onto the tube is difficult to handle, and the inside of the cap may become contaminated while the ointment is being applied. The metal container answers all these objections, for the following reasons: 1. Each metal container is completely sterile. 2. No

part of the tube comes in contact with the patient's eye. 3. A separate sterile container is used for every patient. 4. There is no danger of contaminating the inside of the cap, as it is screwed onto the end of the sterile adjustment rod while the tube is in use. 5. The same tube may be used over and over again until all of its contents has been used up. 6. The tubes may be set up in a battery of a dozen or more containers before a series of dressings are done. 7. The containers fit several of the standard-sized ointment tubes and may be sterilized indefinitely, so that the cost of the dispenser is well offset by its practical applicability.

The dispenser may be obtained from the Werner Surgical Supply Co., 1060 Lexington Avenue, New York.

927 Park Avenue.

THE "INCIDENT NEUTRAL" POINT IN RETINOSCOPY

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NEW YORK

When one speaks of the neutral point in retinoscopy, one ordinarily refers to the point where the emergent rays from the patient's eye meet. This may be called the "emergent neutral" point. But there is another neutral point which concerns the incident light and may be called the "incident neutral" point. The latter neutral point is obtained when one uses a concave mirror (or a concave mirror effect) of intermediate focus. When the incident light is made to focus in the plane of the patient's pupil, there will be neutrality of motion irrespective of any refractive error the patient may have.

One can understand this phenomenon from the basic facts in retinoscopy, without elaborate tracings of rays. A plane or a long focus concave mirror always produces a "with" movement of the light patch on the patient's retina, although it may sometimes appear to move "against." A short focus concave mirror always produces an "against" movement of the light patch on the patient's retina, although this, too, may sometimes appear to move "with." One would expect, therefore, that a concave mirror of intermediate focus such as to bring the incident rays to a focus in the plane of the patient's pupil would produce no movement of the light patch on the patient's retina, irrespective of any refractive error the patient might have.

A simple way to demonstrate this is by the use of some of the modern luminous retinoscopes, with which the light source can be moved nearer to or farther away from the mirror. One can thus, by continuous sliding of the light source, obtain the effect of a plane mirror or of a concave mirror of different focal lengths—long, intermediate and short. Using such a retinoscope, say, on an emmetropic eye and starting with the plane mirror effect, the examiner will note a "with" movement of the reflex. By sliding the light to get a concave mirror effect, he will continue to get a "with" movement until at some stage the movement ceases—and he gets neutrality. By further sliding the light source, he will observe an "against" movement of the reflex. He will thus get reversal of motion in the patient's eye without the interposition of lenses, simply by altering the vergence of the incident rays.

Since movements of the reflex as the physician sees them are occasioned by movements of the light patch on the patient's retina, when there is no movement of the light patch there will be no apparent movement of the reflex. The examiner who unwittingly gets the incident neutral point will see the same retinoscopic phenomena as when he gets the emergent neutral point, though the latter, the really important neutral point for determining the refractive error, may be far off. With an instrument with which concave mirror effects are easily obtained, this is especially likely to happen, as I have seen, to the utter confusion of the physician, who was unaware of the existence of the incident neutral point.

These two neutral points have been called by Professor Marquez the first and second neutral points. But the terms incident neutral and emergent neutral points emphasize more fully their causation and significance. The incident neutral point is caused by the incident light having a certain vergence with reference to the patient, and the emergent neutral point, by the emergent light having a certain vergence with reference to the examiner.

Correspondence

CHRONIC TEARING

To the Editor:—During the past few months following the publication of my article, "Chronic Tearing Cured by Reestablishment of Normal Tear Conduction Passages," in the December 1947 issue of the ARCHIVES, page 775, I have received a number of requests for more detailed information on the use of indwelling horsehair in maintaining the patency of the newly formed punctum and lower canaliculus. Most of these questions are concerned with what precaution need be taken so that the free end of the horsehair at the punctum does not damage the cornea by scratching or by irritating the globe.

I believe it worth while to publish the method that I have been using to obviate this danger since I submitted my article in October 1946.

Should the punctum, as well as the lower canaliculus, be closed by scar tissue, I proceed as follows: The point selected for starting the perforation into the tear sac should be slightly closer to the globe than the site of the original punctum. Comparison with the position of the punctum of the other eye (if normal) aids in correctly selecting the proper point. With the use of local anesthesia, a sharp needle on a holder is pushed through the scar tissue in the direction of the middle of the tear sac until it comes into contact with the bony lacrimal fossa. The lower lid is pulled away from the direction of the needle during the perforating. The needle is then slowly withdrawn to the point of entrance. The direction of the needle is now reversed, and a 3 to 4 mm. counterpuncture is made in the lower lid. This counterpuncture forms a blind pocket, into which the free end of the horsehair is inserted. Increasingly larger, dull-pointed needles, up to the caliber of a no. 6 Bowman probe, are used to dilate the puncture. The direction of this counterpuncture is somewhat backward and downward, being determined by the junction of the inner angle of the bony socket of the eye and the root of the nose. Immediately on withdrawal of the largest dilating needle, the horsehair is inserted as far as possible into the newly formed lower canaliculus. If the horsehair does not seem to have entered deeply enough, it is withdrawn. The dilation is repeated, and a new, stiff piece of horsehair is immediately inserted. A tiny bead is now strung on the horsehair and slid along until it is in contact with the newly formed punctum. This bead maintains the patency of the punctum. The free end of the horsehair is cut so that it fits snugly into the blind pocket prepared for it. After a period of two to three weeks, depending on the individual case, epithelization is complete, and the horsehair with its bead is removed.

Preferable to the use of a bead which slides easily on the horsehair is one that fits tightly, because it better maintains its position at the punctum. Such a bead is prepared as follows: A drop of viscous, liquid "cellophane" is allowed to dry on the horsehair, while it is revolved in all directions to secure roundness. After several days, when the drop is thoroughly dried, the tapering ends are cut off with a glass-cutting steel

file. Rough edges are smoothed with a steel nail file. Such a bead can be slid with some resistance anywhere along the horsehair.

It is possible that sensitivity to horsehair and/or the bead may cause irritation in allergic persons; however, I have not encountered this.

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EFFECT OF LOCALLY APPLIED ANTIHISTAMINE DRUGS ON NORMAL EYES

To the Editor:—Since there has been some interest in the use of the antihistamine drugs locally in the eye, the following data on the ocular tolerance to a group of these compounds, which are reported to have particularly high antihistamine activity, may be of use to persons contemplating therapeutic trials.

The approximate maximum concentrations at which no alteration of the rabbit cornea occurs, as shown by examination with the slit lamp, after application of a single drop of solution are: phenazoline hydrochloride ("antistin hydrochloride," Ciba Pharmaceutical Products, Inc.), 1.5 per cent; diphenhydramine hydrochloride ("benadryl hydrochloride," Parke, Davis & Company), 1 per cent; doxylamine succinate ("decapryn," Wm. S. Merrell Company), 5 per cent; thenylpyramine hydrochloride ("histadyl," Eli Lilly & Co.), 5 per cent; pyranisamine maleate ("neoantergan," Merck & Co., Inc.), 5 per cent; tripelennamine hydrochloride ("pyribenzamine hydrochloride," Ciba Pharmaceutical Products, Inc.), 2.5 per cent; thenylpyramine hydrochloride ("thenylene," Abbott Laboratories), 5 per cent; phenindamine tartrate ("thephorin," Hoffmann-La Roche, Inc.), 1 per cent. At slightly higher concentrations these drugs produce temporary keratitis epithelialis. At still higher concentration corneal edema develops, and there may be loss of epithelium.

The maximum concentrations which are noninjurious to the rabbit cornea cannot be employed in treatment of human eyes because of production of considerable pain. Concentrations which produce approximately the same discomfort as 0.5 per cent tetracaine ("pontocaine") hydrochloride in human eyes, and which might therefore, be considered the maximum dose suitable for clinical use are: "antistin," 0.75 per cent; "benadryl hydrochloride," 0.5 per cent; "decapryn," 1 per cent; "thenylene," 0.4 per cent; "histadyl," 0.75 per cent; "neoantergan," 0.5 per cent; "pyribenzamine," 0.5 per cent, and "thephorin," 0.5 per cent. These values are for solution in 0.9 per cent solution of sodium chloride, with resultant p_H ranging from 5 to 7, with the exception of that for phenindamine tartrate ("thephorin"), which is 3.5. Considerably more concentrated unbuffered solutions of these compounds have nearly the same values of p_H. If these solutions are adjusted to a p_H of 9, all give a considerable precipitate except for "decapryn" and "antistine," both of which produce the same ocular reaction as at p_H 5. When they are adjusted to p_H 8, their effect in normal human eyes does not differ from that of the unbuffered solutions. It appears that discomfort is not attributable to excessive acidity or alkalinity. No perceptible injury is produced at the concentrations noted as suitable for human eyes, but there is in all instances a slight transient conjunctival hyperemia. Only diphenhy-

dramine hydrochloride ("benadryl hydrochloride") has a noticeable mydriatic or cycloplegic effect, and none of the drugs produces noteworthy anesthesia on single application.

No attempt has been made here to assess the penetrative characteristics or relative therapeutic values of these compounds, which, of course, would be determined by many factors in addition to the small differences in local toxicity which have been noted here.

W. MORTON GRANT, M. D., and DONALD R. LOEB, M. D., Boston.

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OVERACTION OF SUPERIOR OBLIQUE MUSCLE

To the Editor:—North American authors frequently do not take notice of, or they overlook, the literature of other countries, especially of Latin America. This may be due to the impediment of language, and sometimes to the inferior place in which they place us in these countries. We also have been seriously criticized on a number of occasions when publications from this part of the continent have bibliographic deficiencies.

In these times, when *Panamericanismo* is not an empty word (as shown by the recent congress at Habana), we of the Western Hemisphere should aim to know one another better and should not consider each other strangers, since we all believe that "it's great to be an American."

I wish to note particularly that Latin-American publications were not mentioned in three recent articles by authors from the United States on subjects on which there was but little literature (Kirby, D. B.: Paralysis of Ocular Elevation With and Without Ptosis, ARCH. OPHTH. **35**:199 [March] 1946. Burian, H. M.: Sensorial Retinal Relationship in Concomitant Strabismus, ibid. **37**:336 [March]; 504 [April]; 618 [May] 1947. Berke, R. N.: Tenotomy of the Superior Oblique Muscle for Hypertropia, ibid. **38**:605 [Nov.] 1947).

Berke states on page 608: "Hughes and Bogart (*Am. J. Ophth.* **25**:911 [Aug.] 1942) are the only authors who have advocated weakening an overacting superior oblique muscle in anomalies of the vertically-acting extraocular muscles." On page 609 he adds: "Tenotomy or tenectomy of the superior oblique muscle has never been performed to relieve hypertropia in a patient with overaction of this muscle." The first assertion is wholly inaccurate; the second also is in error, for if the tenotomy or tenectomy of the superior oblique has not been performed, another operation instead has been successfully carried out. Meesman first (*Klin. Monatsbl. f. Augenh.* **105**:156 [Aug.] 1940) and Malbran later (*Arch. de oftal. de Buenos Aires* **17**:337 [June] 1942) reported on the overaction of the superior oblique and its successful treatment by section of the trochlea. Both articles were published prior to the work of Hughes and Bogart, and neither was mentioned in Hughes's second publication (*Am. J. Ophth.* **27**:1123, 1944).

JORGE MALBRAN, Buenos Aires, Argentina.

Juncal 1330.

SENSITIVITY TO APPLICATION OF SODIUM SULFACETIMIDE

To the Editor:—The absence of allergic manifestations to sodium sulfacetimide when applied to the eye, either as a 30 per cent solution or

as a 10 per cent ointment, has led me to the frequent use of this drug in a large variety of external ocular conditions. Dr. Hedwig Kuhn (Sodium Sulfacetimide 30% Solution in Ophthalmology, *Tr. Am. Acad. Ophth.* **50:**210 [May-June] 1946) stated that ". . . to date, at least, the sodium sulfacetimide preparation [has never shown] an allergic reaction." She warned, however, that it is possible to have an allergic reaction. Benedict and Henderson reported a case of sensitivity to sodium sulfacetimide (*Am. J. Ophth.* **30:**984 [Aug.] 1947). I wish to add another case of sensitivity to this drug.

Miss H. G., a white woman aged 38, was referred to me for a lump on the right lower lid. Examination showed a round, raised, soft, nodular mass, about 4 by 5 mm. in diameter, with a small surrounding area of localized hyperemia. She was told to use hot compresses and was given a prescription for an ointment containing sodium sulfacetimide in 10 per cent concentration. On March 4 the cyst broke spontaneously and discharged through the skin just below the margin of the lid. There was still a slight amount of tenderness. She was told to continue with the application of sodium sulfacetimide and hot compresses. She was seen on March 12, complaining that both the upper and the lower lid had become sore, itchy and painful. Examination revealed a typical allergic dermatitis involving the upper and lower lids of the right eye. She had been using the sodium sulfacetimide ointment faithfully, and she told me at this time that she was allergic to sulfonamide drugs in general. She was instructed to discontinue use of the sulfacetimide ointment and to report back in three days. She called me on March 15 and stated that the dermatitis had cleared up entirely.

I wish to present this case as one of allergy to sodium sulfacetimide. I believe that the drug should be used with caution in the case of a patient who gives a history of sensitivity to other sulfonamide compounds.

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News and Notes

EDITED BY DR. W. L. BENEDICT

GENERAL NEWS

The Revue internationale du trachome.— The organ of the Ligue contre le Trachome, founded in 1923 by Morax and Nicolle, and of the International Organization Against Trachoma, which has appeared in French and in English, will be republished shortly. The officers of the Ligue contre le Trachome are P. Bailliart, president, and Jean Sedán, secretary, 93, rue Sylvabelle, Marseille; and those of the International Organization Against Trachoma are A. F. MacCallan, president, and F. Wibaut, secretary, P. C. Hoofdtraat 145, Amsterdam, Netherlands.

The contents of the first issue of the new series will contain a report of the meeting of the Ligue contre le Trachome (May 21, 1947) and an article by A. F. MacCallan on the ophthalmic campaign in Egypt; Dr. Jean Sedán will report on twenty-five years of action against trachoma and the question of hiring workers with trachoma. The following articles will also appear: "Treatment of Trachoma Overseas," P. Toulant; "Trachoma and the Union Francaise," Roger Nataf; "What Is Known About Trachoma?," E. Delanoë; "Cause of Trachoma," Roger Nataf; "Trachoma," Louis Rostkowski; "Denig's Operation for Trachoma," Noah Pines; "Inefficiency of Para-Aminobenzoic Acid in Treatment of Trachoma" and "Value of Evidence Against the Rickettsial Nature of the Disease," G. B. Bietti and G. Pasca.

Further information may be obtained from Dr. A. F. MacCallan, Westminster Hospital Medical School, 17, Horseferry Road, London.

Alumni Meeting of Institute of Ophthalmology, Presbyterian Hospital, New York.— The alumni meeting of the Institute of Ophthalmology of the Presbyterian Hospital in the City of New York was held on April 30 and May 1. The program consisted of the following papers: "A New Scleral Type of Implant—Motion Picture," Dr. Norman Cutler; "Retinoblastoma: Autopsy Observations," Dr. George R. Merriman; "Determination of Lysozym in Tears," Dr. Ellen Regan; "The Fundus in Pheochromocytoma," Dr. John Cunningham, discussion by Dr. Gordon Bruce; "Preliminary Report on Use of Foreign Protein in Treatment of Intraocular Disease," Dr. Graham Clark; "Experimental Studies on Sympathetic Ophthalmia," Dr. Raymond Collins; "Experimental Results with a New Antibiotic," Dr. Murray Sanders; "Autoroentgenographic Studies on the Eye," Dr. Ludwig von Sallmann; "Clinical Experience with DFP [di-isopropyl fluorophosphate]," Dr. W. Conrad Stone; "Effect of Dicumarol on the Visual Fields in Glaucoma," Dr. William P. McGuire; "Experimental Studies with Antibiotics and Antibiotic Mixtures in Treatment of Intraocular Infections," Dr. John Locke; "Orthoptics—Racket or Cure?" Dr. A. Lloyd Morgan; "Transplantation of Cornea in Keratoconus," Dr. Ramon Castroviejo, and "Investigation on Cases of Retrolental Fibroplasia," Dr. A. C. Unsworth. Demonstra-

tions were made of pupillography by Dr. Otto Lowenstein; gonioscopy by Dr. M. U. Troncoso; physiologic optics by Dr. Hardy, Dr. Rand and Miss Rittler; artificial eyes by Mr. E. G. Bethke, and radiotherapy of retinoblastoma by Dr. George R. Merriam.

***Rivista di oftalmologia* Continued as *Giornale italiano de oftalmologia*.**—The Italian journal *Rivista di oftalmologia* is being continued as the *Giornale italiano de oftalmologia,* under the same editor (Prof. B. Alajmo and collaborators) and the management of the Clinica Oculistica Universitaria of Florence, Italy. The new journal will be issued every two months; its first number has appeared (**1**:1 [Jan.-Feb.], 1948).

The Thigpen-Cater Eye Hospital.—The Thigpen-Cater Eye Hospital, in Birmingham, Ala., is organized on one floor of the Jefferson-Hillman Hospital, and provides for two ophthalmic operating rooms, eighteen beds for ophthalmic patients (ten additional charity beds), a full time photographer, a full time medical artist, orthoptic technician, residents' quarters, laboratory and executive offices for the department and for the Alabama Sight Conservation Association.

Annual Meeting of Wilmer Residents Association.— The annual meeting of the Wilmer Residents Association was held at the Wilmer Ophthalmological Institute on April 14 to 16, 1948. The program consisted of the following papers "Removal of the Eye," Dr. Jack S. Guyton; "A Two Piece Implant," Dr. Charles E. Iliff; "Treatment with Antibiotics and Chemotherapy of Experimental Ocular Tuberculosis," Dr. Alan C. Woods; "Retrolental Fibroplasia," Dr. William C. Owens and Dr. Ella Uhler Owens; "Surgical Treatment of Coarctation of the Aorta and Pulmonic Stenosis," Dr. Alfred Blalock; "Ocular Findings Before and After Operations for Congenital Heart Disease," Dr. Richard A. Hoffman; "Further Studies on Experimental Corneal Transplantation," Dr. Alfred E. Maumenee and Dr. Walter Kornbleuth; "Experimental Use of Heparin in the Eye," Dr. Malcolm W. Bick; "Sterilization of Ophthalmic Solutions," Dr. Samuel D. McPherson Jr. and Dr. Donald Wood; "Nasopharyngeal Carcinoma," Dr. Frank B. Walsh; "Cerebral Representation of the Ocular Movements," Dr. A. Earl Walker; "Enzymatic Histochemistry and Its Application to Ophthalmic Research," Dr. Jonas S. Friedenwald, Dr. Bernard Becker and Miss Jane Crowell; "Results of Cyclodiathermy for Glaucoma," Dr. William G. Marre; "Reabsorption of the Aqueous," Dr. William F. Hughes Jr.; "Recurrent-Erosion of the Cornea," Dr. M. Elliott Randolph; "Compression Tonometry," Dr. Robert A. Moses and Dr. Mary G. Bruno; "The Clinical Pathologic Conference," Dr. Jonas S. Friedenwald and Dr. Robert Day; "Experimental Ocular Histoplasmosis," Dr. Robert Day; "Surgical Treatment of Congenital Cataract," Dr. Cecil Bagley; "Epivascular Choroidal Pigment Streaks: Their Pathology and Medical Prognostic Significance," Dr. Roy O. Scholz; "Long Term Observation of Patients with Retrobulbar or Optic Neuritis," Dr. Robert W. Haines; "Review of Recent Work in Visual Physiology," Dr. Samuel A. Talbot; "Practical Principles in Treatment of Vascular Conditions of the Retina," Dr. Angus L. Mac Lean; "Harada's Disease," Dr. Mary G. Bruno and Dr. Samuel D. Mc

Pherson Jr.; "Synaptic Transmission with Reference to the Retina," Dr. Stephen W. Kuffler; "Bacterial Hypersensitivity and Its Relation to Ocular Disease," Dr. Alan C. Woods and Dr. Ronald Wood.

SOCIETY NEWS

New Officers of Pan-American Association of Ophthalmology.—Dr. Conrad Berens, of New York, was elected president of the Pan-American Association of Ophthalmology at the Third Pan-American Congress of Ophthalmology, held in Habana, Cuba, Jan. 4 to 10, 1948. It was decided to hold the next congress in México, D. F., Mexico, early in 1952.

Twelve vice presidents were elected at the Habana meeting, the representation being based on the number of ophthalmologists in each of the member countries. Those elected were as follows: Argentina, Dr. Esteban Adrogue, Buenos Aires; Bolivia, Dr. Aniceto Solares, Sucre; Brazil, Dr. Ivo Correa Meyer, Porto Alegre; Canada, Dr. John MacMillan, Montreal; Chile, Dr. Santiago Barrenechea, Santiago; Columbia, Dr. Francisco Varnaza, Bogotá; Costa Rica, Dr. Alexis Aguero, San José; Cuba, Dr. Miguel Branly, Habana; Ecuador, Dr. J. M. Varas Samaniego, Guayaquil; Guatemala, Dr. José Miguel Medrano, Guatemala City; United States, Dr. Frederick C. Cordes, San Francisco, and Dr. William L. Benedict, Rochester, Minn. Dr. Moacyr E. Alvaro, Sao Paulo, Brazil, was reelected secretary for the countries south of Panama, and Dr. Thomas D. Allen, Chicago, was elected to succeed Dr. Berens for the corresponding position for the countries north of Panama. The following were appointed assistant secretaries: Dr. Brittain F. Payne, New York; Dr. Jorge Balba, Buenos Aires; Dr. Manoel A. da Silva, Sao Paulo, and Dr. F. Palomino Dena, México, D. F., Mexico.

The congress adopted "statutes and by-laws," establishing the Pan-American Association of Ophthalmology as a continuing organization, with the objectives of fostering the progress of ophthalmology, establishing contacts among ophthalmologists of the Western Hemisphere and promoting measures to conserve eyesight and prevent blindness among the peoples of the hemisphere. To achieve these aims, permanent committees were established to deal with the following matters, among others: encouragement of research, glaucoma, trachoma, lighting and optics, contact lens center, orthoptics, prevention of blindness, neuro-ophthalmology, legal and industrial ophthalmology, standardization of ophthalmic hospitals and clinics, inter-American medical relationships, establishment and guidance of ophthalmologic societies and scientific cinematography.

The statutes provide for an Inter-American Federation of Ophthalmologic Societies and for a Bureau of Professors of Ophthalmology, who are to encourage the formation of centers for graduate study and stimulate the teaching of ophthalmology throughout the hemisphere, to effect interchanges of professors and alumni among teaching centers, to arrange for and manage prizes and scholarships and to arrange for examinations of, and issue certificates of proficiency to, physicians who seek them. In the last-mentioned function, the bureau's activities are not intended to interfere with independent examining boards already functioning efficiently.

A board of censors was formed to supervise the relations of Association members to the lay press. According to the resolution adopted at

Habana, local representatives of the Association's press relations committee must approve publication of articles in the lay press concerning any member.

New York Society for Clinical Ophthalmology.—The New York Society for Clinical Ophthalmology recently elected the following officers for the year 1948-1949: president, Dr. Benjamin Esterman; vice president, Dr. Sidney A. Fox;; recording secretary, Dr. Bernard Kronenberg; corresponding secretary, Dr. Leon H. Ehrlich; treasurer, Dr. Edward Saskin; historian, Dr. Howard J. Agatston; committee chairmen, Dr. Adolph Posner (program), Dr. Frederick H. Theodore (instruction hour), Dr. Max Chamlin (legislative), Dr. Bernard Fread (membership), Dr. David A. Newman (industrial). Dr. Daniel Kravitz, the retiring president was elected to the advisory council.

Ophthalmological Journal Club.—A meeting was held at the home of Dr. Samuel V. Abraham, 610 North Linden Drive, Beverly Hills, Calif., April 15, 1948, for the purpose of organizing the Ophthalmological Journal Club.

The primary interest of the club is to abstract current literature on ophthalmology and related subjects for the purpose of presenting it to the members for discussion.

The meetings will be held the first Thursday of each month at 8 p. m., at 416 Bedford Drive, Beverly Hills, Calif.

Dr. Samuel V. Abraham will be chairman of the club.

Book Reviews

Clinical Neuro-Ophthalmology. By Frank B. Walsh, M. D., F. R. C. S. (Edin.). Price, $18. Pp. 1,532, with 384 illustrations. Baltimore: The Williams & Wilkins Company, 1947.

In recent years great advances have been made in neuro-ophthalmology, and knowledge of the intricate central connections of the ocular apparatus has been much advanced. An up-to-date treatise is therefore most timely, and this has been accomplished by Dr. Walsh with this monumental work of 1,532 pages, which is an exhaustive and systematic exposition of neuro-ophthalmology, with particular emphasis on the clinical side.

One of the great difficulties in a work of this kind is a proper classification. Dr. Walsh has been much influenced by the outline used by Dr. F. R. Ford in his "Diseases of the Nervous System in Children" and has chosen a classification which is based on etiology, with due emphasis on clinical features.

In the first chapter, on the "Visual Pathways and the Diagnosis of Lesions Situated at Different Levels," the subject is divided into the following parts: (1) anatomy; (2) arrangement of visual fibers in the optic pathway; (3) topical diagnosis of the visual pathways, with particular reference to the visual fields; (4) topical diagnosis of lesions in the higher visual pathways; aphasia; apraxia; agnosia; alexia.

The second chapter describes the other cranial nerves and the topical diagnosis of their lesions. This is followed by chapters on the following subjects: the autonomic system; the pupil: normal and abnormal accommodation; the eyelids and extraocular muscles; papilledema, optic neuritis: optic atrophy; congenital and developmental abnormalities and diseases of the eyes and central nervous system; infections and parasitic invasions of the nervous system and their ocular signs, including an outline of the nervous system and ocular syphilis; heredofamilial and degenerative disease; toxic and metabolic diseases; disorders of muscles; vascular lesions and circulatory disorders of the nervous system: ocular signs; ocular and intracranial tumors and related conditions; injuries by physical agents: ocular signs; epilepsy, migraine and other paroxysmal disorders; ocular signs of hysteria, malingering and traumatic neurosis: the psychiatric aspects of ocular disorders (Dr. M. Levin); drugs, poisons and toxic amblyopias.

These titles indicate the thorough manner in which the subject has been treated, and the reader is soon impressed with the completeness of the work and the vast amount of information it contains. In a subject as difficult as neurologic diagnosis a detailed description of the basic sciences is desirable, and this has been included in the text of each chapter. Many case reports are added to illustrate the variability and the problems of differential diagnosis. At the end of each chapter there is a list of references which, without claiming to be complete, is designed to facilitate further study. There are 384 illustrations. An index of 108 pages completes the volume and brings also a list of the case histories.

To Dr. Walsh are due our hearty congratulations on the completion of this colossal task, the importance of which is signified by the manifold interest of its contents, as well as by the author's deep study and long experience, at both the Johns Hopkins and the Baltimore City Hospital.

The book presents a complete outline of the subject and will serve as a valuable reference book. The illustrations and print are admirable, but the book is rather heavy to handle and its length is somewhat formidable.

ARNOLD KNAPP.

Transactions of the Ophthalmological Society of Australia (British Medical Association).—Volume 6. Price, 15 S. Pp. 155. Sydney, Australia: Australasian Medical Publishing Company, Ltd., 1946.

These *Transactions* record the proceedings of the Australian Ophthalmological Society at its sixth annual meeting held on Oct. 23, 1946, in Melbourne. The president was J. R. Anderson, whose presidential address, "Our Common Enemy, Blindness," occupies more than 25 per cent of the volume. Following this are two papers by the guest of honor, Air Commodore P. C. Livingston, of the Royal Air Force. In the first of these, "Experiences in Night Vision in the Royal Air Forces," he recounts the development of testing methods in use in the R. A. F. He discriminates between the perception of light minimum (an elementary difference in threshold discrimination) and variations in the power to synthesize form. The latter was obviously the more important, and so the well known rotating hexagon was devised. It is fully described and illustrated in the paper. It was further found that the scotopic field varied considerably from the field obtained at photopic levels. All scotopic fields demonstrated a round or oval central absolute scotoma, and it was often possible to plot the roots and main branches of the retinal vessels. In the second paper, "Heterophoria in Aircrew: Its Clinical and Psychological Significance," Livingston describes the development and technic of investigative procedures and the significance of the findings. He expresses the belief that many persons with heterophoria fly successfully, and also that many fail but succeed later when the heterophoria is corrected. He is convinced that there are two basic types of heterophoria: first, the type for which the child learns to compensate by experience and, second, the variety which follows illness or fatigue.

The subject of orthoptic treatment is continued by Diana S. Mann out of a considerable experience with private, public and Air Force patients. She states her belief that orthoptic treatment has never straightened a constantly convergent pair of eyes. She has never been able to obtain stereoscopic vision when a squint had become constant under the age of 1 year. If binocular vision has never existed, it can never be developed. She has obtained her best results in dealing with eyestrain that did not respond to correction of refractive error, and, to a lesser extent, she is encouraged by her results in convergence deficiency.

Nutritional disases in prisoners of war are discussed in papers by S. Gerstman ("A Survey of Retrobulbar Neuritis in Prisoners of War"), by C. Colvin ("Ocular Disturbances Associated with Malnutrition") and by R. Maynard ("Blindness Among Prisoners of War"). Gerstman is skeptical of temporal pallor and recommends use of the 2 and 4 meter screens for mapping central scotomas. He thinks that the prognosis in such cases is not encouraging. Colvin points out that ocular symptoms in

malnutrition are slow in appearing and states that of persons in the same area and receiving the same diet, some will exhibit ocular symptoms and others will not. Maynard reports on the pathologic sections of two globes enucleated from patients with gross malnutrition. The sections illustrated a diffuse demyelinating lesion of the optic nerve, combined with degeneration of the ganglion cells and nerve fibers of the internal layers of the retina.

In a short article, entitled "The Future of Australian Ophthalmology," K. O'Day points out that most Australian ophthalmologists had been trained in England and indicates the advisability of establishing faculties for such training at home.

J. Maude reports a case of "angioid streaks of the retina and pseudoxanthoma elasticum." This disease must be much rarer in Australia than it is in the United States, where numerous examples of the syndrome have been reported. It is unfortunate that Maude's bibliography does not include the paper by Grönblad, who first detected the relation of the two diseases.

In his paper, entitled "Inherited Retinal Detachment," J. B. Hamilton has compiled a pedigree of sufferers from this disease. He examined 10 patients and found that pseudoglioma and retinal cysts were peculiar features, aniridia was a complication, hypermetropia was the invariable rule and no history of trauma was ever elicited. He is convinced that congenital cystic disease of the retina in its infantile form may be, like congenital cystic disease of the lung, part of a generalized cystic process throughout the body.

The interest in the effect of maternal rubella on the infantile eye continues to be high in the country where the work originated. E. O. Marks ("Pigmentary Abnormality in Children Congenitally Deaf Following Maternal German Measles") examined the children in a school for the blind and deaf. Nearly half the deaf children born in the epidemic years showed marked pigmentary abnormalities resembling atypical retinitis pigmentosa. Those born in other years had normal fundi. Of 38 deaf children with a history of maternal rubella, 17 had abnormally pigmented fundi. Of 37 deaf children with abnormally pigmented fundi, 21 had a history of maternal rubella.

"Intracapsular Cataract Extraction: Its Most Serious Complication" is the title of a paper by F. Roberts. The complication is a progressive contraction upward of the pillars of the iris due to the formation of a fibrous tissue band in the ciliary body above.

Continuing his work on glaucoma due to trauma, A. D'Ombrain ("Concussion Glaucoma") has reached a conclusion as to the etiologic mechanism of the condition. He states the belief that sufficient trauma may cause fibrosis of the ciliary region or the venous capillary bed.

In the final paper the "Choice of Operation in Glaucoma," by N. Macindoe, the author counsels repeated paracentesis in cases of corneal ulcer, lime burns and severe hyphema complicating secondary glaucoma. With dislocation of the lens, he prefers a posterior sclerotomy before the lens is removed, and in cases of iris bombé he advises iridectomy. In cases of acute primary glaucoma, he suggests a posterior sclerotomy, followed by a filtering operation. In dealing with chronic glaucoma, he prefers iridencleisis in cases in which a subsequent cataract operation is planned and in which the patient is old and has advanced glaucoma. If the eye is quiet, he performs trephination; if it is not, he does a Lagrange operation.

G. M. Bruce.